10/551,931

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=> d his

     (FILE 'HOME' ENTERED AT 15:47:34 ON 03 JAN 2008)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
L1         14054 S BLOOD (W)SUBSTITUT?
L2          4447 S HEMOGLOBIN (6W) ALBUMIN
L3           105 S L1 AND L2
L4            68 DUP REM L3 (37 DUPLICATES REMOVED)
L5            43 S HB(2W)HSA
L6            12 DUP REM L5 (31 DUPLICATES REMOVED)
                 E SU Z/AU
L7             0 S S E3
L8           957 S  E3
                 E XIULING L/AU
L9             7 S E3
                 E CHUNYANG Z/AU
L10            1 S E3
                 E YUHONG X/AU
L11            3 S E3
L12          968 S L8 OR L9 OR L10 OR L11
L13           77 S L4 OR L6
L14            0 S L12 AND L13
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NEWS 3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS 4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS 5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
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NEWS 25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS 26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS 27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS 28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
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NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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FILE 'LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
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=> s blood (w) substitut?
L1 14054 BLOOD (W) SUBSTITUT?

=> s hemoglobin (6w) albumin
L2 4447 HEMOGLOBIN (6W) ALBUMIN

=> s l1 and l2
L3 105 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 68 DUP REM L3 (37 DUPLICATES REMOVED)

=> d ibib ab

L4 ANSWER 1 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:193529 HCAPLUS
DOCUMENT NUMBER: 146:259144
TITLE: Methods for exchange of carbon monoxide and oxygen

coordinated to complexes and ligand exchange apparatus for the methods
INVENTOR(S): Takeoka, Shinji; Suzuki, Daisuke; So, Keitaro; Tsuchida, Hidetoshi
PATENT ASSIGNEE(S): Oxygenix Co., Ltd., Japan; Waseda University
SOURCE: Jpn. Kokai Tokkyo Koho, 12pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2007045718	A	20070222	JP 2005-229222	20050808

PRIORITY APPLN. INFO.: JP 2005-229222 20050808

AB Solution containing complexes coordinated by CO is fed from the upper part of a tilted liquid membrane support to form a liquid membrane and the liquid membrane is fluidized to the lower side of the support while passing O-containing gas through the support and irradiating the liquid membrane with visible light to recover the complexes coordinated by O from the lower part of the support. Solution containing complexes coordinated by O is fed to the upper part of the support and the formed liquid membrane is fluidized to the lower side of the support while passing gas containing ≤0.1% O through the support to recover solution of O-free complexes from the lower part of the support. Also claimed is a ligand exchange apparatus for the above methods having (a) a tilted gas-permeable support, (b) a opening to feed the solution to the support, (c) an inlet and an outlet for the O-containing or O-free gas, and (d) an opening to recover the solution after ligand exchange. These simple and highly-effective methods using the apparatus are useful for manufacture of artificial oxygen carriers containing e.g. Hbs, albumins, etc. Thus, cotton fabric was stretched on an acrylic container tilted at 15° and a dispersion of phospholipid small vesicles containing carbonyl-Hb was fed from the upper side of the support under visible light irradiation and feed of O gas to give Hb with rate of CO coordination 19%.

=> d his

(FILE 'HOME' ENTERED AT 15:47:34 ON 03 JAN 2008)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
L1 14054 S BLOOD (W)SUBSTITUT?
L2 4447 S HEMOGLOBIN (6W) ALBUMIN
L3 105 S L1 AND L2
L4 68 DUP REM L3 (37 DUPLICATES REMOVED)

=> d -168 ibib ab

L4 ANSWER 1 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:193529 HCAPLUS
DOCUMENT NUMBER: 146:259144
TITLE: Methods for exchange of carbon monoxide and oxygen coordinated to complexes and ligand exchange apparatus for the methods
INVENTOR(S): Takeoka, Shinji; Suzuki, Daisuke; So, Keitaro; Tsuchida, Hidetoshi
PATENT ASSIGNEE(S): Oxygenix Co., Ltd., Japan; Waseda University
SOURCE: Jpn. Kokai Tokkyo Koho, 12pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2007045718	A	20070222	JP 2005-229222	20050808

PRIORITY APPLN. INFO.: JP 2005-229222 20050808

AB Solution containing complexes coordinated by CO is fed from the upper part of a tilted liquid membrane support to form a liquid membrane and the liquid membrane is fluidized to the lower side of the support while passing O-containing gas through the support and irradiating the liquid membrane with visible light to recover the complexes coordinated by O from the lower part of the support. Solution containing complexes coordinated by O is fed to the upper part of the support and the formed liquid membrane is fluidized to the lower side of the support while passing gas containing ≤0.1% O through the support to recover solution of O-free complexes from the lower part of the support. Also claimed is a ligand exchange apparatus for the above methods having (a) a tilted gas-permeable support, (b) a opening to feed the solution to the support, (c) an inlet and an outlet for the O-containing or O-free gas, and (d) an opening to recover the solution after ligand exchange. These simple and highly-effective methods using the apparatus are useful for manufacture of artificial oxygen carriers containing e.g. Hbs, albumins, etc. Thus, cotton fabric was stretched on an acrylic container tilted at 15° and a dispersion of phospholipid small vesicles containing carbonyl-Hb was fed from the upper side of the support under visible light irradiation and feed of O gas to give Hb with rate of CO coordination 19%.

L4 ANSWER 2 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:635438 HCAPLUS
DOCUMENT NUMBER: 147:38270
TITLE: Rheological Properties of Hemoglobin Vesicles (Artificial Oxygen Carriers) Suspended in a Series of Plasma-Substitute Solutions
AUTHOR(S): Sakai, Hiromi; Sato, Atsushi; Takeoka, Shinji; Tsuchida, Eishun
CORPORATE SOURCE: Advanced Research Institute for Science and Engineering and Graduate School of Science and Engineering, Waseda University, Tokyo, 169-8555, Japan
SOURCE: Langmuir (2007), 23(15), 8121-8128
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hb vesicles (HbV) or liposome-encapsulated Hbs are artificial oxygen carriers that have been developed for use as transfusion alternatives. The extremely high concentration of the HbV suspension (solutes, ca.16 g/dL; volume fraction, ca.40 volume %) gives it an oxygen-carrying capacity that is comparable to that of blood. The HbV suspension does not possess a colloid osmotic pressure. Therefore, HbV must be suspended in or co-injected with an aqueous solution of a plasma substitute (water-soluble polymer), which might interact with HbV. This article describes our study of the rheol. properties of HbV suspended in a series of plasma substitute solns. of various mol. wts.: recombinant human serum albumin (rHSA), dextran (DEX), modified fluid gelatin (MFG), and hydroxyethyl starch (HES). The HbV suspended in rHSA was nearly Newtonian. Other polymers-HES, DEX, and MFG-induced HbV flocculation, possibly by depletion interaction, and rendered the suspensions as non-Newtonian with a shear-thinning profile (10-4-103 s-1). These HbV suspensions showed a high storage modulus (G') because of the presence of flocculated HbV. However, HbV suspended in

rHSA exhibited a very low G'. The viscosities of HbV suspended in DEX, MFG, and high-mol.-weight HES solns. responded quickly to rapid step changes in shear rates of 0.1-100 s-1 and a return to 0.1 s-1, indicating that flocculation is both rapid and reversible. Microscopically, the flow pattern of the flocculated HbV that perfused through microchannels (4.5 μm deep, 7 μm wide, 20 cmH2O applied pressure) showed no plugging. Furthermore, the time required for passage was simply proportional to the viscosity. Collectively, the HbV suspension viscosity was influenced by the presence of plasma substitutes. The HbV suspension provides a unique opportunity to manipulate rheol. properties for various clin. applications in addition to its use as a transfusion alternative.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 68 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1

ACCESSION NUMBER: 2007:286919 BIOSIS
DOCUMENT NUMBER: PREV200700290156
TITLE: The role of pH and its control on effective conjugation of bovine hemoglobin and human serum albumin
AUTHOR(S): Zheng, Chunyang; Ma, Guanghui; Su, Zhiguo [Reprint Author]
CORPORATE SOURCE: Chinese Acad Sci, Natl Key Lab Biochem Engn, Inst Proc Engn, POB 353, Beijing 100080, Peoples R China
zgsu@home.ipe.ac.cn
SOURCE: Process Biochemistry, (MAR 2007) Vol. 42, No. 3, pp. 303-309.
ISSN: 1359-5113.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 2007
Last Updated on STN: 2 May 2007

AB Human serum albumin (HSA) and bovine hemoglobin (Hb) conjugate is a promising candidate as a blood substitute. However, preparation of the conjugate is problematic because both proteins tend to conjugate between themselves rather than crosslink each other. In this work, a facile process for conjugation of Hb and HSA was developed through control strategy of the reaction. The reaction was carried out in a buffer containing borax-borate and mannite. The borax-borate was used for pH buffering while mannite was used as a pH switch and a reaction promoter. As a result, self-conjugation of Hb and self-conjugation of HSA were minimized. After the one-step conjugation reaction in aqueous solution, followed by the one-step purification by ion-exchange chromatography, the conjugate of HSA and Hb was obtained with the total yield about 50%. The P-50 and the Hill coefficient for the product were 16.1 mmHg and 1.82, respectively. (c) 2006 Elsevier Ltd. All rights reserved.

L4 ANSWER 4 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:896074 HCAPLUS
DOCUMENT NUMBER: 147:284799
TITLE: Cerebral oxygen delivery by liposome-encapsulated hemoglobin: a positron-emission tomographic evaluation in a rat model of hemorrhagic shock
AUTHOR(S): Awasthi, Vibhudutta; Yee, Seong-Hwan; Jerabek, Paul; Goins, Beth; Phillips, William T.
CORPORATE SOURCE: Department of Radiology, University of Texas Health Science Center at San Antonio, San Antonio, TX, USA
SOURCE: Journal of Applied Physiology (2007), 103(1), 28-38
CODEN: JAPHEV; ISSN: 8750-7587
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Liposome-encapsulated Hb (LEH) is being developed as an artificially

assembled, low-toxicity, and spatially isolated Hb-based oxygen carrier (HBOC). Standard methods of evaluating oxygen carriers are based on surrogate indicators of physiol. in animal models of shock. Assessment of actual delivery of oxygen by HBOCs and resultant improvement in oxygen metabolism at the tissue level has been a tech. challenge. In this work, we report our findings from 15O-positron emission tomog. (15O-PET) evaluation of LEH in a rat model of 40% hypovolemic shock. In vitro studies showed that PEGylated LEH formulation containing .apprx.7.5% Hb and consisting of neutral lipids (distearoylphosphatidylcholine:cholesterol:α-tocopherol, 51.4:46.4:2.2) efficiently picks up 15O-labeled oxygen gas. The final preparation of LEH contained 5% human serum albumin to provide oncotic pressure. Cerebral PET images of anesthetized rats inhaling 15O-labeled O2 gas showed efficient oxygen-carrying and delivery capacity of LEH formulation. From the PET images, we determined cerebral metabolic rate of oxygen (CMRO2) as a direct indicator of oxygen-carrying capacity of LEH as well as oxygen delivery and metabolism in rat brain. Compared with control fluids [saline and 5% human serum albumin (HSA)], LEH significantly improved CMRO2 to .apprx.80% of baseline level. Saline and HSA resuscitation could not improve hypovolemia-induced decrease in CMRO2. On the other hand, resuscitation of shed blood was the most efficient in restoring oxygen metabolism The results suggest that 15O-PET technol. can be successfully employed to evaluate potential oxygen carriers and blood substitutes and that LEH resuscitation in hemorrhage enhances oxygen delivery to the cerebral tissue and improves oxygen metabolism in brain.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1337827 HCAPLUS
DOCUMENT NUMBER: 146:68521
TITLE: PEGylated hemoglobin and albumin for blood substitutes
INVENTOR(S): Acharya, Seetharama A.; Manjula, Belur N.
PATENT ASSIGNEE(S): Albert Einstein College of Medicine of Yeshiva University, USA
SOURCE: PCT Int. Appl., 59pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006135740	A1	20061221	WO 2006-US22463	20060609

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-689175P P 20050610

AB The present invention provides PEGylated Hbs and PEGylated albumins comprising polyethylene glycol (PEG) conjugated to Hb or to albumin, wherein the PEG is a maleimide PEG, an alkylamide PEG, an iodoacetamide PEG, a p-nitrothiophenyl PEG, a vinyl sulfone PEG, or a mixed disulfide PEG. The PEGylated albumins and

PEGylated Hbs comprise polyethylene glycol (PEG) attached to a thiolated amino group of albumin or Hb, wherein the amino group is thiolated using dithiosulfosuccinimidyl propionate (DTSSP) or dithiosuccinimidyl propionate (DTSP) or dithiobispropionimidate. The invention also provides methods of preparing PEGylated Hbs and PEGylated albumins comprising (a) reacting Hb or albumin with a thiolating agent and with a PEGylating agent, and (b) capping unPEGylated reactive thiols of Hb or albumin with N-ethylmaleimide. The invention further provides compns. and blood substitutes comprising PEGylated Hbs and PEGylated albumins.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:629172 HCAPLUS
DOCUMENT NUMBER: 145:109815
TITLE: Production of artificial blood using molecular assembling science
AUTHOR(S): Takeoka, Shinji
CORPORATE SOURCE: Fac. Sci. Eng., Waseda University, Tokyo, 169-8555, Japan
SOURCE: Jinko Ketsueki (2006), Volume Date 2005, 13(4)., 136-147
CODEN: JIKEFK; ISSN: 1341-1594
PUBLISHER: Nippon Ketsueki Daitaibutsu Gakkai
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review. This manuscript was a summary of the Presidential Lecture of the 12th Annual Meeting of the Society of Blood Substitutes, Japan, which was held at International Conference Center, Waseda University, July 6-7th, 2005. We have been studying the production of artificial blood (red blood cell substitutes, platelet substitutes) by utilizing the basic knowledge and application of mol. assembling science such as interaction between Hb or albumin and amphiphiles phospholipids. This manuscript introduces 1.Production of Hb Vesicles (HbV) as red blood cell substitutes, 2. Production of nanoparticles (polymerized albumin, phospholipid vesicles) bearing recognition sites as platelet substitutes, and 3. Design of intelligent nanoparticles.

L4 ANSWER 7 OF 68 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005603850 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16024576
TITLE: Extreme hemodilution with PEG-hemoglobin vs. PEG-albumin.
AUTHOR: Cabrales Pedro; Tsai Amy G; Winslow Robert M; Intaglietta Marcos
CORPORATE SOURCE: La Jolla Bioengineering Institute, 505 Coast Blvd. S., Suite 405, La Jolla, CA 92037, USA.. pcabrales@ucsd.edu
CONTRACT NUMBER: HL-R01-40696 (NHLBI)
HL-R01-62318 (NHLBI)
HL-R01-62354 (NHLBI)
HL-R24- 64395 (NHLBI)
SOURCE: American journal of physiology. Heart and circulatory physiology, (2005 Dec) Vol. 289, No. 6, pp. H2392-400. Electronic Publication: 2005-07-15.
Journal code: 100901228. ISSN: 0363-6135.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 15 Nov 2005
Last Updated on STN: 11 Jan 2006
Entered Medline: 10 Jan 2006

AB Isovolemic hemodilution to 11% systemic hematocrit was performed in the hamster window chamber model using 6% dextran 70 kDa (Dx 70) and 5% human serum albumin (HSA). Systemic and microvascular effects of these solutions were compared with polyethylene glycol (PEG)-conjugated 5% albumin (MPA) and PEG-conjugated 4.2% Hb (MP4). These studies were performed for the purpose of comparing systemic and microvascular responses of PEG vs. non-PEG plasma expanders and similar oxygen-carrying vs. noncarrying blood replacement fluids. Mean arterial blood pressure was statistically significantly reduced for all groups compared with baseline ($P < 0.05$), HSA, MPA, and MP4 higher than Dx 70 ($P < 0.05$). MP4 and MPA had a significantly higher cardiac index than HSA and Dx 70, in addition to a positive base excess. Microvascular blood flow and capillary perfusion were significantly higher for the PEG compounds compared with HSA and Dx 70. Intravascular PO2 for MP4 and MPA was higher in arterioles ($P < 0.05$) compared with HSA and Dx 70, but there was no difference in either tissue or venular PO2 between groups. Total Hb in the MP4 group was 4.8 +/- 0.4 g/dl, whereas the remaining groups had a range of 3.6-3.8 g/dl. The hemodilution results showed that PEG compounds maintained microvascular conditions with lower concentrations than conventional plasma expanders. Furthermore, microvascular oxygen delivery and extraction in the window chamber tissue were significantly higher for the PEG compounds. MP4 was significantly higher than MPA ($P < 0.05$) and was not statistically different from baseline, an effect due to the additional oxygen release to the tissue by the Hb MP4.

L4 ANSWER 8 OF 68 EMBASE DUPLICATE 3
ACCESSION NUMBER: 2006009097 EMBASE
TITLE: Replacement of rat blood with conjugate of hemoglobin and human serum albumin.
AUTHOR: Lu X.-L.; Ma T.-M.; Zheng C.-Y.; Wang Y.-Q.; Shi X.-D.; Suo X.-Y.; Yu P.-Z.; Xu Y.-H.; Su Z.-G.
CORPORATE SOURCE: Z.-G. Su, National Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing 100080, China. zgsu@home.ipe.ac.cn
SOURCE: Chinese Pharmaceutical Journal, (Oct 2005) Vol. 40, No. 19, pp. 1510-1513.
Refs: 9
ISSN: 1001-2494 CODEN: ZYZAEU
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
LANGUAGE: Chinese
SUMMARY LANGUAGE: English; Chinese
ENTRY DATE: Entered STN: 26 Jan 2006
Last Updated on STN: 26 Jan 2006

AB OBJECTIVE: To study the effect of replacement of rat blood with the conjugate of bovine hemoglobin and human serum albumin (Hb-HSA conjugate) and other resuscitation fluids on the blood pressure and survival. METHODS: 30% or 60% of whole blood was replaced with Hb-HSA conjugate, ringer-lactate, solution, stroma-free hemoglobin (SFHb), 5% HSA in Ringer-lactate respectively. Whole blood replacement was used in blank control group and no resuscitation fluid was supplied in negative control group. Mean arterial pressure (MAP) was continuously recorded throughout the experiment. All rats were monitored for 14 d. RESULTS: For both 30% and 60% blood replacement, ringer-lactate and 5% HSA in ringer-lactate increased the MAP to a level lower than the baseline. Hb-HSA conjugate, the same as whole blood, maintains the MAP. While SFHb increased the MAP from (132.2 ± 4.0)mmHg to (139.3 ± 4.1) mmHg in 30% replacement

group, but only sustained the blood pressure in the first 10 min and then decreased to lower level than the initial level in 60% replacement group. The Hb-HSA conjugate showed effectiveness with 100% survival rate (followed for 14 d), as well as whole blood replacement. CONCLUSION: The pressure change in 30% bleeding rats is more sensitive to the resuscitation fluids. The Hb-HSA conjugate maintains the MAP of bleeding rats and effectively saved bleeding rats, prior to other resuscitation fluids. The results indicate that the product is able to be a candidate as blood substitute in emergency.

L4 ANSWER 9 OF 68 MEDLINE on STN
ACCESSION NUMBER: 2005437942 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16104545
TITLE: Preliminary report: effects of artificial blood on hypoxic pulmonary vasoconstriction.
AUTHOR: Oshima Yoshiaki; Okazaki Naoto
CORPORATE SOURCE: Department of Anesthesiology, Shimane Prefectural Central Hospital, Izumo 693-8555.
SOURCE: Masui. The Japanese journal of anesthesiology, (2005 Aug) Vol. 54, No. 8, pp. 898-900.
Journal code: 0413707. ISSN: 0021-4892.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 18 Aug 2005
Last Updated on STN: 8 Oct 2005
Entered Medline: 7 Oct 2005

AB BACKGROUND: We examined the effects of artificial blood on hypoxic pulmonary vasoconstriction (HPV). METHODS: Pump-perfused rabbit lungs were reperfused and ventilated with a mixture of 21% O2, 5% CO2, and balance N2. HPV was induced by reduction of O2 concentration from 21 to 3% for 5 min. Pulmonary arterial pressure (PAP) was measured using a low-pressure transducer. Two perfusion solutions, (1) a mixture of autologous red blood cells and physiological salt solution supplemented with 5% albumin and (2) artificial red blood cells (liposome-encapsulated hemoglobin) and physiological saline supplemented with 5% albumin, were made. Using each solution, HPV was evaluated by PAP increase with and without inhalation of nitric oxide (NO). RESULTS: (1) With both autologous and artificial perfusion solutions, hypoxic stimulation (HS) increased PAP. (2) With the autologous solution, NO inhalation suppressed the HS-induced PAP increase, but with the artificial solutions no such a phenomenon was observed. CONCLUSIONS: NO inhalation failed to suppress HPV with the artificial solution, probably since the liposome-encapsulated hemoglobin strongly inactivated NO.

L4 ANSWER 10 OF 68 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 4
ACCESSION NUMBER: 2005:497191 BIOSIS
DOCUMENT NUMBER: PREV200510264943
TITLE: Conjugate of bovine hemoglobin and human serum albumin as a candidate for blood substitute: Characteristics and effects on rats (vol 33, pg 2, 2005).
AUTHOR(S): Liu, Xiu-Ling [Reprint Author]; Zheng, Chun-Yang; Shi, Xiao-Dong; Wang, Yong-Quan; Suo, Xiao-Yan; Yu, Peng-Zhang; Xu, Yu-Hong; Ma, Tie-Min; Su, Zhi-Guo
CORPORATE SOURCE: Chinese Acad Sci, Inst Proc Engn, Natl Key Lab Biochem Engn, Beijing, Peoples R China
SOURCE: Artificial Cells Blood Substitutes and Biotechnology, (2005) Vol. 33, No. 3, pp. 377.
ISSN: 1073-1199.

DOCUMENT TYPE: Article
Errata
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005

L4 ANSWER 11 OF 68 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005383065 EMBASE
TITLE: Erratum: Conjugate of bovine hemoglobin and human serum albumin as a candidate for blood substitute: Characteristics and effects on rats (Artificial Cells, Blood Substitutes and Biotechnology (2005) 33, 2).
AUTHOR: Lu X.-L.; Zheng C.-Y.; Shi X.-D.; Wang Y.-Q.; Suo X.-Y.; Yu P.-Z.; Xu Y.-H.; Ma T.-M.; Su Z.-G.
CORPORATE SOURCE: X.-L. Lu, National Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, China
SOURCE: Artificial Cells, Blood Substitutes, and Immobilization Biotechnology, (2005) Vol. 33, No. 3, pp. 377.
ISSN: 1073-1199 E-ISSN: 1532-4184 CODEN: ABSBE4
COUNTRY: United States
DOCUMENT TYPE: Journal; Errata; (Erratum)
FILE SEGMENT: 025 Hematology
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Sep 2005
Last Updated on STN: 15 Sep 2005

L4 ANSWER 12 OF 68 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2005312309 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15960074
TITLE: Conjugate of bovine hemoglobin and human serum albumin as a candidate for blood substitute: characteristics and effects on rats.
AUTHOR: Lu Xiu-Ling; Zheng Chun-Yang; Xiao-DongShi; Wang Yong-Quan; Suo Xiao-Yan; Yu Peng-Zhan; Xu Yu-Hong; Ma Tie-Min; Su Zhi-Guo
CORPORATE SOURCE: National Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, China.
SOURCE: Artificial cells, blood substitutes, and immobilization biotechnology, (2005) Vol. 33, No. 2, pp. 83-99.
Journal code: 9431307. ISSN: 1073-1199.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 18 Jun 2005
Last Updated on STN: 8 Oct 2005
Entered Medline: 7 Oct 2005

AB Conjugate of bovine hemoglobin (bHb) and human serum albumin (HSA) was prepared. The product was simply composed of 89.7% one-to-one Hb-HSA conjugate, 6.0% oligomer of Hb and HSA, 3.5% unconjugated HSA and 0.8% unconjugated Hb, with an average molecular weight of 157 kD. The physicochemical characteristics were determined. Effects of single replacement on blood pressure and long-term survival of rats with 30% and 60% acute blood loss were studied, in comparison with Ringer-lactate solution, stroma-free hemoglobin (SFHb), 5% HSA in Ringer-lactate, whole blood and no resuscitation fluid. Results showed that Hb-HSA conjugate maintained the mean arterial pressure of rats to initial level with no pressor effect. Long-term effects of the

replacement fluids on 30% bleeding rats showed that, for the group infused with Hb-HSA conjugate, histology of five major organs, heart, kidney, liver, spleen and lung, were essentially normal, similar to that of whole blood, while obviously renal side-effects appeared in other groups. The efficacy of the conjugate was further demonstrated by the resuscitation of lethal hemorrhagic shock rats (60% acute blood loss) with 100% survival rate (followed for 14 days), the same result as whole blood. The Hb-HSA conjugate can thus be another candidate for blood substitute in emergency.

L4 ANSWER 13 OF 68 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 6

ACCESSION NUMBER: 2005:332078 SCISEARCH
THE GENUINE ARTICLE: 907PQ
TITLE: Oxygen infusions (hemoglobin-vesicles and albumin-hemes) based on nano-molecular sciences
AUTHOR: Tsuchida E (Reprint); Sakai H; Komatsu T; Takeoka S; Huang Y B
CORPORATE SOURCE: Waseda Univ, Adv Res Inst Sci & Engn, Tokyo 1698555, Japan (Reprint); Keio Univ, Sch Med, Dept Surg, Tokyo 1608582, Japan
eishun@waseda.jp
COUNTRY OF AUTHOR: Japan
SOURCE: POLYMERS FOR ADVANCED TECHNOLOGIES, (FEB-MAR 2005) Vol. 16, No. 2-3, Sp. iss. SI, pp. 73-83.
ISSN: 1042-7147.
PUBLISHER: JOHN WILEY & SONS LTD, THE ATRIUM, SOUTHERN GATE, CHICHESTER PO19 8SQ, W SUSSEX, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 58
ENTRY DATE: Entered STN: 31 Mar 2005
Last Updated on STN: 31 Mar 2005

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Since the discovery of a red-colored saline solution of a heme derivative that reversibly binds and releases oxygen (1983), significant efforts have been made to realize an oxygen infusion as a red cell substitute based on the sciences of both molecular assembling phenomena and macromolecular metal complexes. The authors have specified that hemoglobin (Hb)-vesicles (HbV) and recombinant human serum albumin-hemes (rHSA-heme) would be the best systems that meet the clinical requirements. (A) Hb is rigorously purified from outdated, donated red cells via pasteurization and ultrafiltration, to completely remove blood type antigen and pathogen. The HbV encapsulates thus purified concentrated Hb solution with a phospholipid bimolecular membrane (diameter, 250 nmo), and its solution properties can be adjusted comparable with blood. Surface modification of HbV with a water-soluble polymer ensures stable dispersion state and storage over a year at 20 degrees C. In vivo tests have clarified the efficacy for extreme hemodilution and resuscitation from hemorrhagic shock, and safety in terms of biodistribution, metabolism in reticuloendothelial system (RES), clinical chemistry, blood coagulation, etc. The HbV does not induce vasoconstriction thus maintains blood flow and tissue oxygenation. (B) rHSA is now manufactured in Japan as a plasma-expander. The rHSA can incorporate eight heme derivatives (axial base substituted hemes) as oxygen binding sites, and the resulting rHSA-heme is a totally synthetic O-2-carrier. Hb binds endothelium-derived relaxation factor, NO, and induces vasoconstriction. The rHSA-heme binds NO as Hb does, however, it does not induce vasoconstriction due to its low pI (4.8) and the resulting low permeability across the vascular wall (1/100 of Hb). A 5%-albumin solution possesses a physiologic oncotic pressure. Therefore, to increase the O-2-transporting capacity, albumin dimer is effective. Albumin dimer can incorporate totally 16 hemes with a regulated oncotic pressure. The rHSA-heme is effective not only as a red cell substitute but also for

oxygen therapeutics (e.g. oxygenation for tumor). Significant efforts have been made to produce HbV and rHSA-heme with a facility of Good Manufacturing Practice (GMP) standard, and to start preclinical and finally clinical trials. Copyright (c) 2005 John Wiley S Sons, Ltd.

L4 ANSWER 14 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:961886 HCAPLUS
DOCUMENT NUMBER: 142:108979
TITLE: Human Serum Albumin Bearing Covalently Attached Iron(II) Porphyrins as O2-Coordination Sites
AUTHOR(S): Wang, Rong-Min; Komatsu, Teruyuki; Nakagawa, Akito; Tsuchida, Eishun
CORPORATE SOURCE: Advanced Research Institute for Science and Engineering, Waseda University, Shinjuku, Tokyo, 169-8555, Japan
SOURCE: Bioconjugate Chemistry (2005), 16(1), 23-26
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:108979
AB Tetrakis{(α,α,α,α-o-pivalamido)phenyl}porphinatoiron(II) with a bifunctional tail possessing an axially coordinated imidazolyl group and a protein attachable succinimidyl(glutamyl) group (FeP-GluSu) has been synthesized. It can efficiently react with the lysine residues of recombinant human serum albumin (rHSA), giving a new albumin-heme conjugate [rHSA(FeP-Glu)]. MALDI-TOF MS showed a distinct mol. ion peak at m/z 70 643, which indicates that three FeP-Glu mols. were covalently linked to the rHSA scaffold. The binding number of FeP-Glu is approx. three (mol/mol) and independent of the mixing ratio. The CD spectrum and Native PAGE revealed that the albumin structure remained unaltered after the covalent bonding of the hemes. This rHSA(FeP-Glu) conjugate can bind and release O2 reversibly under physiol. conditions (pH 7.3, 37°) in the same manner as Hb and myoglobin. The O2-adduct complex had a remarkably long lifetime (τ1/2: 5 h). The O2-binding affinity [P1/2O2: 27 Torr] was identical to that of human red cells. Laser flash photolysis expts. gave the O2- and CO-association rate consts. and suggested that there are two different geometries of the imidazole binding to the central ion.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:265588 HCAPLUS
DOCUMENT NUMBER: 142:422872
TITLE: Red blood cell substitutes: Past, present, and future
AUTHOR(S): Chang, Thomas Ming Swi
CORPORATE SOURCE: Artificial Cells & Organs Research Centre, MSSS-FRSQ Research Group on Blood Substitutes in Transfusion Medicine, Faculty of Medicine, McGill University, Montreal, QC, H3G 1Y6, Can.
SOURCE: Keio University International Symposia for Life Sciences and Medicine (2005), 12(Artificial Oxygen Carrier), 22-33
CODEN: KUISB7
PUBLISHER: Springer Tokyo
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. PolyHb is already well into the final stages of clin. trials in humans. One has been approved for routine clin. use in South Africa. Perfluorochems. are chemical oxygen carriers that are being actively developed with some in the advanced stages of clin. trials. Meanwhile, new generations of modified Hb are being developed that can modulate the effects of nitric oxide. Other systems are also being developed to

include antioxidant properties for those clin. applications that may have potential problems related to oxygen radicals. Other products in advanced stages of animal testing are based on Hb-lipid vesicles, heme-albumin and heme-lipid vesicles. A further development is the use of nanotechnol. and biodegradable copolymers to prepare nano-dimension artificial red blood cells containing Hb and complex enzyme systems.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:265587 HCAPLUS
DOCUMENT NUMBER: 143:292072
TITLE: Safety and efficacy of hemoglobin-vesicles and albumin-hemes
AUTHOR(S): Kobayashi, K.; Horinouchi, H.; Watanabe, M.; Izumi, Y.; Teramura, Y.; Nakagawa, A.; Huang, Y.; Sou, K.; Sakai, H.; Komatsu, T.; Takeoka, S.; Tsuchida, E.
CORPORATE SOURCE: Department of Surgery, School of Medicine, Keio University, Tokyo, 160-8582, Japan
SOURCE: Keio University International Symposia for Life Sciences and Medicine (2005), 12(Artificial Oxygen Carrier), 1-21
CODEN: KUISB7
PUBLISHER: Springer Tokyo
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Keio University and Waseda University have worked together on artificial O2 carrier research for 20 years in close cooperation. Two candidate materials were selected from the viewpoints of safety, efficacy, and cost performance. One is Hb-vesicles (HbV) and the other is albumin-heme (rHSA-heme). This chapter summarizes the authors' video presentation that introduced the recent results of the authors' research into HbV and rHSA-heme.
REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:878298 HCAPLUS
DOCUMENT NUMBER: 141:320134
TITLE: Hemoglobin conjugate and the preparation method and its use
INVENTOR(S): Su, Zhiguo; Lu, Xiuling; Zheng, Chunyang; Xu, Yuhong
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089404	A1	20041021	WO 2004-CN91	20040202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CN 1535986	A	20041013	CN 2003-109622	20030409

CN 1767851	A	20060503	CN 2004-80009102		20040202
US 2006247423	A1	20061102	US 2005-551931		20051005
PRIORITY APPLN. INFO.:			CN 2003-109622	A	20030409
			WO 2004-CN91	W	20040202

AB Present invention provides a Hb and human serum albumin conjugate and its preparation The conjugates has Mr of between 100-300KD, comprising 1-3 Hb mols. crosslinked intermolecularly or intramolecularly and 1-3 human serum albumin mols., which gained by following steps: prepared stroma-free Hb, then coupled Hb to human serum albumin and purified products using anion exchange chromatog. The protein conjugate could be used as a blood substitute.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:915771 HCAPLUS

DOCUMENT NUMBER: 142:341743

TITLE: Comparison of PEG-modified albumin and hemoglobin in extreme hemodilution in the rat

AUTHOR(S): Winslow, Robert M.; Lohman, Jeff; Malavalli, Ashok; Vandegriff, Kim D.

CORPORATE SOURCE: Sangart, and Department of Bioengineering, University of California, San Diego, CA, 92121, USA

SOURCE: Journal of Applied Physiology (2004), 97(4), 1527-1534 CODEN: JAPHEV; ISSN: 8750-7587

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have reported a new polyethylene glycol (PEG)-modified, Hb-based O2 carrier (MP4) with novel properties, including a large mol. excluded volume and low Pot necessary to obtain 50% O2 (.apprx.6 Torr). To evaluate the ability of MP4 to transport O2, we compared it with PEG-modified albumin (MPA) using the identical chemical of attachment of PEG chains. The resulting solns. were well matched with respect to all phys. properties except that MP4 is an O2 carrier, whereas MPA is not. An addnl. solution, 10% pentastarch, was matched with the PEG-modified proteins with regard to oncotic activity and viscosity but does not contain PEG. The model used to evaluate O2 transport was continuous exchange transfusion in the rat until the hematocrit was virtually unmeasureable. Objective end points included survival and the onset of anaerobic metabolism, signaled by acid-base derangement and accumulation of lactic acid. Continuous exchange transfusion of 2.5 blood vols. in rats (n = 5 in each treatment group) was carried out over 60 min, such that the final hematocrit was between 0 and 5% in all animals. Animals were observed for an addnl. 70 min, when survivors were killed. Overall survival for the MP4 animals was 100%; no animal that received either pentastarch or MPA survived. The hematocrit at which lactic acid began to rise was .apprx.14.8% in both pentastarch and MPA animals and 7.4% in the animals that received MP4. In all groups, the total Hb was .apprx.5 g/dL at this point. We conclude that, despite its low Po2 necessary to obtain 50% O2. MP4 effectively substitutes for red blood cell Hb in its ability to oxygenate tissues in extreme hemodilution.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:231036 HCAPLUS

DOCUMENT NUMBER: 141:354929

TITLE: Rheological properties of PEG-modified Hb-vesicles (HbVs) and their oxygen-transporting capacity in vivo

AUTHOR(S): Sakai, Hiromi; Sou, Keitaro; Takeoka, Shinji; Kobayashi, Koichi; Tsuchida, Eishun

CORPORATE SOURCE: Advanced Research Institute for Science and Engineering, Waseda University, Tokyo, 169-8555, Japan

SOURCE: PMSE Preprints (2004), 90, 580
CODEN: PPMRA9; ISSN: 1550-6703
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; (computer optical disk)
LANGUAGE: English

AB PEG-modified Hb vesicles suspended in recombinant human serum albumin showed no aggregation and appropriate viscosity similar with blood and were effective for restoration from hemorrhagic shock that is comparable with shed autologous blood.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 68 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004056107 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14758176
TITLE: Hemoglobin-vesicles suspended in recombinant human serum albumin for resuscitation from hemorrhagic shock in anesthetized rats.
AUTHOR: Sakai Hiromi; Masada Yohei; Horinouchi Hirohisa; Yamamoto Manabu; Ikeda Eiji; Takeoka Shinji; Kobayashi Koichi; Tsuchida Eishun
CORPORATE SOURCE: Advanced Research Institute for Science and Engineering, Waseda University, Tokyo, Japan.
SOURCE: Critical care medicine, (2004 Feb) Vol. 32, No. 2, pp. 539-45.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 4 Feb 2004
Last Updated on STN: 31 Mar 2004
Entered Medline: 30 Mar 2004

AB OBJECTIVE: Hemoglobin-vesicle (HbV) has been developed to provide oxygen-carrying ability to plasma expanders. Its ability to restore the systemic condition after hemorrhagic shock was evaluated in anesthetized Wistar rats for 6 hrs after resuscitation. The HbV was suspended in 5 g/dL recombinant human serum albumin (HbV/rHSA) at an Hb concentration of 8.6 g/dL. DESIGN: Prospective, randomized, controlled trial. SETTING: Department of Surgery, School of Medicine, Keio University. SUBJECTS: Forty male Wistar rats. INTERVENTIONS: The rats were anesthetized with 1.5% sevoflurane inhalation throughout the experiment. Polyethylene catheters were introduced through the right jugular vein into the right atrium for infusion and into the right common carotid artery for blood withdrawal and mean arterial pressure monitoring. MEASUREMENTS AND MAIN RESULTS: Shock was induced by 50% blood withdrawal. The rats showed hypotension (mean arterial pressure = 32 +/- 10 mm Hg) and significant metabolic acidosis and hyperventilation. After 15 mins, they received HbV/rHSA, shed autologous blood (SAB), washed homologous red blood cells (wRBC) suspended in rHSA (wRBC/rHSA, [Hb] = 8.6 g/dL), or rHSA alone. The HbV/rHSA group restored mean arterial pressure to 93 +/- 8 mm Hg at 1 hr, similar to the SAB group (92 +/- 9 mm Hg), which was significantly higher compared with the rHSA (74 +/- 9 mm Hg) and wRBC/rHSA (79 +/- 8 mm Hg) groups. There was no remarkable difference in the blood gas variables between the resuscitated groups; however, two of eight rats in the rHSA group died before 6 hrs. After 6 hrs, the rHSA group showed significant ischemic changes in the right cerebral hemisphere relating to the ligation of the right carotid artery followed by cannulation, whereas the HbV/rHSA, SAB, and wRBC/rHSA groups showed less changes. CONCLUSIONS: HbV suspended in recombinant human serum albumin provides restoration from hemorrhagic shock that is comparable with that using shed autologous blood.

L4 ANSWER 21 OF 68 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2004386571 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15229746
TITLE: Second-generation recombinant hemoglobin molecules do not stimulate sphincter of Oddi, gallbladder or duodenal motility in the Australian brush-tailed possum.
AUTHOR: Takahata Shunichi; Konomi Hiroyuki; Schloithe Ann C; Toouli James; Saccone Gino T P
CORPORATE SOURCE: Department of General and Digestive Surgery, Centre for Neuroscience and the Centre for Digestive Science, Flinders University, Flinders Medical Centre, Bedford Park, South Australia, Australia.
SOURCE: Canadian journal of gastroenterology = Journal canadien de gastroenterologie, (2004 Jul) Vol. 18, No. 7, pp. 441-8. Journal code: 8807867. ISSN: 0835-7900.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 5 Aug 2004
Last Updated on STN: 27 Oct 2004
Entered Medline: 26 Oct 2004

AB BACKGROUND: Several studies have investigated the effects of hemoglobin-based oxygen carriers on gastrointestinal motility. Diaspirin cross-linked hemoglobin reduces sphincter of Oddi trans-sphincteric flow and increases duodenal motility in the Australian brush-tailed possum, effects attributed to nitric oxide (NO) scavenging. Recently, second-generation recombinant hemoglobin molecules with reduced NO scavenging ability have been developed. AIM: To determine the effects of two second-generation recombinant hemoglobin solutions and the prototype recombinant hemoglobin with high NO binding, on duodenal and biliary motility in the Australian brush-tailed possum. METHOD: Blood pressure; duodenal, sphincter of Oddi and gallbladder motility; and trans-sphincteric flow were recorded. The effects of recombinant hemoglobin or human serum albumin (control) solutions on these parameters were investigated. Each solution was infused intravenously at 1 mL/kg/min to deliver 250 mg/kg or 500 mg/kg. RESULTS: Duodenal contraction frequency was stimulated by the high dose of prototype recombinant hemoglobin, but not by a comparable dose of second-generation recombinant hemoglobin. The induced duodenal activity occurred in the later phase of the experimental period. In contrast, biliary motility and trans-sphincteric flow were not altered by any hemoglobin solution. The high dose of all the hemoglobin solutions elevated blood pressure, whereas the low dose solutions did not alter any parameter measured. CONCLUSION: At the doses studied, the second-generation recombinant hemoglobin with reduced NO binding capacity did not significantly alter duodenal and biliary motility, supporting the need for further studies to evaluate their potential usefulness as blood substitutes.

L4 ANSWER 22 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:911037 HCAPLUS
DOCUMENT NUMBER: 142:169572
TITLE: Resuscitation from hemorrhagic shock with MalPEG-albumin: comparison with MalPEG-hemoglobin
AUTHOR(S): Wettstein, Reto; Cabrales, Pedro; Erni, Dominique; Tsai, Amy G.; Winslow, Robert M.; Intaglietta, Marcos
CORPORATE SOURCE: Department of Bioengineering, University of California, La Jolla, CA, USA
SOURCE: Shock (2004), 22(4), 351-357
CODEN: SAGUAI; ISSN: 1073-2322
PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Our aim was to determine the efficacy of polyethylene glycol-conjugated human albumin (MaIPEG-Alb) in restoring circulatory volume after 1 h of hemorrhagic shock. Expts. were performed in the awake condition in the hamster skin fold preparation Microhemodynamic parameters and tissue PO2 were assessed with intravital microscopy and the use of the phosphorescence quenching technique. One hour after shock induction by withdrawal of 50% of the blood volume, animals were resuscitated with MaIPEG-Alb (n = 6). Systemic and microhemodynamic parameters following resuscitation were identical to those obtained with the same protocol using MaIPEG-Hb. However, parameters related to microvascular oxygen distribution were significantly lower in the MaIPEG-Alb group compared with the previous data from the MaIPEG-Hb group in that tissue oxygen partial pressure was 5 ± 2 mmHg (vs. 8 ± 3 mmHg, $P < 0.05$), oxygen delivery was reduced to 60 ± 27% ($P < 0.05$), and oxygen consumption was reduced to 69 ± 28% ($P < 0.05$). Both mols. were matched in composition (4.2 g/dL) and surface chemical MaIPEG-Alb colloid osmotic pressure was 37 mmHg (vs. 49 mmHg for MaIPEG-Hb), and viscosity was 2.7 cP (vs. 2.5 cP for MaIPEG-Hb). The present results show that both solns. are efficacious plasma expanders and that the Hb-based solution provides improved oxygen distribution and tissue PO2 in the hamster chamber model.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:638137 HCAPLUS
DOCUMENT NUMBER: 142:140872
TITLE: Evaluation of safety and efficacy of hemoglobin-vesicles and albumin -hemes
AUTHOR(S): Tsuchida, Eishun
CORPORATE SOURCE: Advanced Research Institute for Science and Engineering, Waseda University, Tokyo, 169-8555, Japan
SOURCE: International Journal of the Society of Materials Engineering for Resources (2004), 12(1), 1-11
CODEN: IMEREB; ISSN: 1347-9725
PUBLISHER: Society of Materials Engineering for Resources of Japan
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Since the discovery of a red-colored saline solution of a heme derivative that reversibly binds and releases O2 (1983), significant efforts have been made to realize an O2 infusion as a red cell substitute based on the sciences of both mol. assembling phenomena and macromol. metal complexes. We have specified that Hb-vesicles (HbV) and recombinant human serum albumin -hemes (rHSA-hemes) would be the best systems that meet the clin. requirements. The HbV encapsulates ultrapure concentrate Hb solution, that is free of any infectious elements, with a phospholipid bimol. membrane (diameter, 250 nmϕ), and its solution properties can be adjusted comparable with blood. Surface modification of HbV with a water-soluble polymer ensures stable dispersion state and storage over a year at 20. In vivo tests have clarified the efficacy for extreme hemodilution and resuscitation from hemorrhagic shock, and safety in terms of biodistribution, metabolism in RES, clin. chemical, blood coagulation, etc. The HbV does not induce vasoconstriction thus maintains blood flow and tissue oxygenation. The rHSA-heme is a totally synthetic O2 carrier that incorporates 8 heme derivs. (axial base substituted hemes) as O2 binding sites in the hydrophobic pockets of rHSA, which is now manufactured in Japan as a plasma-expander. Hb binds endothelium-derived relaxation factor, NO, and induces vasoconstriction. The rHSA-heme binds NO as Hb does, however, it does not induce vasoconstriction due to its low pI (4.8) and the resulting low permeability across the vascular wall (1/100 of Hb). A

5%-albumin solution possesses a physiol. oncotic pressure. Therefore, to increase the O2-transporting capacity, albumin dimer is effective. Albumin dimer can incorporate totally 16 hemes with a regulated oncotic pressure. The rHSA-heme is effective not only as a red cell substitute but also for O2 therapeutics (e.g., oxygenation for tumor). Significant efforts have been made to produce HbV and rHSA-hemes with a facility of GMP standard, and to start preclin. and finally clin. trials.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:10180 HCAPLUS
DOCUMENT NUMBER: 138:44660
TITLE: Electrochemical method for deoxidation of oxygen-containing solutions
INVENTOR(S): Tsuchida, Hidetoshi; Takeoka, Shinji; Huang, Yu-bin
PATENT ASSIGNEE(S): Japan Science and Technology Corporation, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003001257	A	20030107	JP 2001-190302	20010622
JP 3442751	B2	20030902		
PRIORITY APPLN. INFO.:			JP 2001-190302	20010622

AB The method involves introducing O-containing sample solns. containing electrolytes into the cathode chamber separated from the anode chamber via an ion-permeable porous diaphragm, introducing electrolyte solns. into the anode chamber, and passing elec. current while passing mixed gas containing H and N through the electrolyte solns. The O-containing solns. may contain O carriers such as Hbs and metalloporphyrins. Dissolved O was completely removed from aqueous soln's. or dispersions containing albumin, concentrated Hb, or Hb vesicles without contamination of the solns.

L4 ANSWER 25 OF 68 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 9
ACCESSION NUMBER: 2002:609680 BIOSIS
DOCUMENT NUMBER: PREV200200609680
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules.
AUTHOR(S): Hsia, Jen-Chang [Inventor]
CORPORATE SOURCE: ASSIGNEE: Synzyme Technologies, Inc.
PATENT INFORMATION: US 6458758 20021001
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct. 1, 2002) Vol. 1263, No. 1. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Nov 2002
Last Updated on STN: 27 Nov 2002

AB Compositions and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiologically compatible macromolecules. In particular, hemoglobin-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free hemoglobin solutions, encapsulated hemoglobin solutions, stabilized hemoglobin solutions, polymerized hemoglobin solutions, conjugated hemoglobin

solutions, nitroxide-labelled albumin, and nitroxide-labelled immunoglobulin. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, particularly in cerebral ischemia in stroke, and in vivo enzyme mimics among others.

L4 ANSWER 26 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:239340 HCAPLUS
DOCUMENT NUMBER: 137:10803
TITLE: Bovine serum albumin-bovine hemoglobin conjugate as a candidate blood substitute
AUTHOR(S): Hu, Tao; Su, Zhiguo
CORPORATE SOURCE: National Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China
SOURCE: Biotechnology Letters (2002), 24(4), 275-278
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A bovine serum albumin-bovine Hb conjugate was prepared using 3-maleimidobenzoic acid N-hydroxysuccinimide ester as cross-linker. The conjugate was purified using DEAE Sepharose. It had an Mr of 127 kDa. Its P50 (half-saturated O2 pressure) value and Hill coefficient were 27 mm Hg and 2, resp.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:419943 HCAPLUS
DOCUMENT NUMBER: 138:33066
TITLE: Albumin extravasation and tissue washout of hyaluronan after plasma volume expansion with crystalloid or hypooncotic colloid solutions
AUTHOR(S): Berg, S.; Golster, M.; Lisander, B.
CORPORATE SOURCE: Department of Anesthesiology and Intensive Care, University Hospital, Linkoping, Swed.
SOURCE: Acta Anaesthesiologica Scandinavica (2002), 46(2), 166-172
CODEN: AANEAB; ISSN: 0001-5172
PUBLISHER: Blackwell Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Intravascular volume expansion is followed by loss of fluid from the circulation. The extravasation of albumin in this readjustment is insufficiently known. Twelve male volunteers participated, each in three sep. sessions, in a controlled, randomized, open fashion. They received one of the following: albumin 40 g/L, (7.1 mL/kg, i.e., 500 mL per 70 kg); Ringer's acetate (21.4 mL/kg), or dextran 30 g/L (7.1 mL/kg). The fluids were infused during 30 min and the subjects were followed for 180 min. ECG, arterial oxygen saturation and non-invasive arterial pressure were recorded. Hb, hematocrit, serum albumin and osmolality, plasma colloid osmotic pressure and hyaluronan concentration were determined in venous samples. The serum albumin concentration decreased ($P < 0.05$, ANOVA) following Ringer's acetate or dextran, whereas serum osmolality was unchanged in all groups. The colloid osmotic pressure decreased ($P < 0.05$) after the Ringer solution The blood volume increase was estimated from the decrease in Hb concentration and did not differ between the three fluids. The

cumulated extravasation of albumin was largest following albumin (10.4 ± 5.4 g, mean ± SD), less following dextran (5.6 ± 5.0 g) and negligible in the Ringer group (0.5 ± 10.0 g; $P < 0.05$ against albumin). However, the Ringer solution increased the plasma concentration of hyaluronan drastically. Thus, infusion of hypotonic colloidal solns. entails net loss of albumin from the vascular space. This is not the case after Ringer's acetate. Increased interstitial hydration from the latter fluid is followed by lymphatic wash out of hyaluronan.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:31257 HCAPLUS
DOCUMENT NUMBER: 134:83105
TITLE: Continuous cardiac perfusion preservation with PEG-Hb for improved hypothermic storage
INVENTOR(S): Serna Danny, L., Jr.; Milliken, Jeffrey C.; Purdy, Ralph E.
PATENT ASSIGNEE(S): Regents of the University of California, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001001774	A1	20010111	WO 2000-US16895		20000619
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1207753	A1	20020529	EP 2000-942962		20000619
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
US 2007243518	A1	20071018	US 2007-712829		20070228
PRIORITY APPLN. INFO.:			US 1999-139819P	P	19990617
			US 1999-143709P	P	19990714
			WO 2000-US16895	W	20000619
			US 2002-18534	B1	20021107

AB The proposed use of the invention is for the ex vivo preservation of human and animal donor organ allografts during transportation from the donor to the recipient for the purpose of transplantation. In addition to its use for ex vivo myocardial preservation, this PEG-Hb solution has tremendous potential utility for in vivo myocardial preservation during open heart surgery as well as a blood substitute or blood replacement during or following surgery of any sort, including open heart surgery. The invention comprises a PEG coated bovine Hb based solution for the purpose of ex vivo donor organ preservation and the use of the same. The fundamental principle of the solution is to provide an oxygen, nutritional and electrolyte environment to the tissue of the donor organ that is conducive to ex vivo preservation such that the donor organ will regain acceptable function post transplantation. The solution provides oxygen, a carbohydrate energy source, continuous metabolite washout and continuous perfusion with an isotonic, normokalemic, hypocalcemic solution that drastically improves myocardial preservation over current techniques considered the standard of care. Donor organ preservation for transplantation is performed using ischemic hypothermic immersion storage in saline solution using hypothermic perfusion preservation with an oxygen carrying Hb solution

The solution contains PEG-Hb, human albumin, dextrose, heparin sodium, lidocaine-HCl, $MgSO_4$, KCl, $CaCl_2$, THAM, NaCl, $NaHCO_3$, Na_3PO_4, without which PEG-Hb is lethal to the myocardium and cannot be used for the purpose of effective organ preservation. Thus, continuous perfusion preservation of rabbit hearts for 8 h with PEG-Hb at 30 mmHg and 20° gave left ventricular function that was superior to 8-h perfusion with a chemical similar crystalloid solution without addition of PEG-Hb, despite similar myocardial edema. Extended cardiac perfusion preservation with PEG-Hb may be useful in transplantation.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 29 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:765019 HCAPLUS
DOCUMENT NUMBER: 134:227192
TITLE: Protective effects of plasma replacement fluids on erythrocytes exposed to mechanical stress
AUTHOR(S): Sumpelmann, R.; Schurholz, T.; Marx, G.; Zander, R.
CORPORATE SOURCE: Zentrum Anasthesiologie, Medizinische Hochschule Hannover, Hannover, 30625, Germany
SOURCE: Anaesthesia (2000), 55(10), 976-979
CODEN: ANASAB; ISSN: 0003-2409
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hb release from 40 suspensions of packed red blood cells in modified fluid gelatin, 4% albumin solution, 6% hydroxyethyl starch and normal saline was investigated in vitro during circulation with a roller pump from a heart-lung machine for 120 min at a flow rate of 2.5 l.min-1 at room temperature The lowest Hb release was obtained with erythrocytes in modified fluid gelatin, whereas free Hb concns. became progressively higher with albumin, hydroxyethyl starch and normal saline [median free Hb (interquartile range) after 120 min circulation: gelatin 493 (360-601) mg.l-1, albumin 692 (590-1111) mg.l-1, hydroxyethyl starch 1121 (692-1518) mg.l-1, normal saline 1178 (881-1757) mg.l-1, $p < 0.001$]. Modified fluid gelatin appears to have potent erythrocyte protective properties similar to those of albumin. This effect could decrease mech. hemolysis during extracorporeal circulation or cell saver autotransfusion if modified fluid gelatin is used as part of a priming solution or as an additive in wash solns.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:815916 HCAPLUS
DOCUMENT NUMBER: 134:80696
TITLE: Resuscitative effects of polynitroxylated αα-cross-linked hemoglobin following severe hemorrhage in the rat
AUTHOR(S): Buehler, Paul W.; Mehendale, Sangeeta; Wang, Huashan; Xie, Jingtian; Ma, Li; Trimble, Charles E.; Hsia, Carleton J. C.; Gulati, Anil
CORPORATE SOURCE: Department of Pharmaceutics and Pharmacodynamics, The University of Illinois, Chicago, IL, 60612, USA
SOURCE: Free Radical Biology & Medicine (2000), 29(8), 764-774
CODEN: FRBMEH; ISSN: 0891-5849
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB αα-Cross-linked Hb (ααHb) is an example of a Hb-based oxygen carrier (HBOC) with significant cardiovascular activity. This may compromise the safety and efficacy of this HBOC by causing

systemic hypertension and reducing blood flow to some organs. The present work is based on the hypothesis that incorporating antioxidant activity into an HBOC in the form of a covalently attached nitroxide may prevent these effects. The authors have tested this hypothesis by adding antioxidant activity to αα Hb with 2,2,6,6-tetramethyl-piperidinyl-1-oxyl (Tempo) to create polynitroxylated αα Hb (PN-αα Hb). The new compound PN-αα Hb acts as an antioxidant in the authors in vitro and in vivo assays. In this study urethane-anesthetized rats were hemorrhaged to a mean arterial pressure (MAP) of 35-40 mmHg and maintained for 30 min. Animals were resuscitated with solns. of (1) 10% PN-αα Hb (43 mmHg), (2) 10% αα Hb (43 mmHg), (3) 7.5% albumin (43 mmHg), (4) 300% Ringers lactate (RL), and (5) 0.9% normal saline equal to the shed blood volume (SBV). Hemodynamics and regional blood circulation was measured at baseline, following hemorrhage, and at 30 and 60 min postresuscitation using a radioactive microsphere technique. Base deficit (BD) was measured at baseline, following hemorrhage, and at 60 min following resuscitative fluid infusion. Finally survival was determined as the time following resuscitation until secession of heart rhythm. Saline and 300% RL resuscitation did not improve BD, systemic hemodynamics, or regional blood circulation. PN-αα Hb, αα Hb, and albumin significantly improved these parameters, however, only PN-αα Hb and αα Hb improved survival. PN-αα Hb was less hypertensive than αα Hb due to blunted increases in both cardiac output and systemic vascular resistance. This study demonstrates that, by using αα Hb as a scaffold for polynitroxylation, improvement in vasoactivity and resuscitative efficacy may be possible. In conclusion, the addition of antioxidant activity in the form of polynitroxylation of a low mol. weight Hb (αα Hb) may create a safe and efficacious resuscitative fluid.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 68 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 10

ACCESSION NUMBER: 1999:450406 SCISEARCH
THE GENUINE ARTICLE: 205LU
TITLE: Plasma volume expansion with solutions of hemoglobin, albumin, and Ringer lactate in sheep
AUTHOR: Fischer S R (Reprint); Burnet M; Traber D L; Prough D S; Kramer G C
CORPORATE SOURCE: UTMB, Dept Anesthesiol, Galveston, TX 77555 USA (Reprint); Shriners Burns Inst, Galveston, TX 77555 USA
COUNTRY OF AUTHOR: USA
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY-HEART AND CIRCULATORY PHYSIOLOGY, (JUN 1999) Vol. 276, No. 6, pp. H2194-H2203. ISSN: 0363-6135.
PUBLISHER: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36
ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We have measured plasma volume expansion (Evans blue and hematocrit changes) and hemodynamic responses in conscious hemorrhaged and normovolemic splenectomized sheep after a 30-min infusion of either 20 ml/kg of diaspirin cross-linked hemoglobin (DCLHb), 20 ml/kg of human albumin (Alb), or 60 ml/kg of a solution of Ringer lactate (RL). All regimens expanded blood volume and increased blood pressure and cardiac output after hemorrhage. However, only 15 +/- 3% of the infused volume of RL was evident as intravascular expansion 10-min postinfusion,

compared with 67 +/- 16% and 139 +/- 139% for Alb and DCLHb, respectively. DCLHb infusions were associated with higher blood pressures and lower cardiac outputs compared with RL and Alb infusions, but the increased oxygen content of blood with DCLHb resulted in systemic delivery of oxygen similar to that of the other infusions. These differences in hemodynamics and vascular volume continued for 6 h, and at 24 h vascular volume and all hemodynamics were similar in all three groups. The better volume expansion with DCLHb may be due to greater mobilization of endogenous interstitial protein or reduced transcapillary loss as total intravascular endogenous plasma protein increased after infusion of DCLHb, whereas there was an apparent loss of endogenous intravascular protein after infusions of Alb and RL. Vasoconstriction by DCLHb is one mechanism that could lower blood-to-tissue transport of fluid and protein. In addition to its oxygen-carrying capacity and vasoactivity, DCLHb is associated with volume expansion properties out of proportion to its colloid osmotic pressure.

L4 ANSWER 32 OF 68 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1999375187 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10444491
TITLE: Modified hemoglobins produce venular interendothelial gaps and albumin leakage in the rat mesentery.
AUTHOR: Baldwin A L
CORPORATE SOURCE: Department of Physiology, College of Medicine, University of Arizona, Tucson, Arizona 85724-5051, USA.. abaldwin@u.arizona.edu
CONTRACT NUMBER: HL-53047-04 (NHLBI)
SOURCE: The American journal of physiology, (1999 Aug) Vol. 277, No. 2 Pt 2, pp. H650-9.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 5 Oct 1999
Last Updated on STN: 5 Oct 1999
Entered Medline: 23 Sep 1999

AB Cross-linked hemoglobin (alphaalpha-Hb) and polyethylene glycol (PEG)-conjugated Hb have both been considered as possible "blood substitutes." Previously, we showed that PEG-Hb extravasates rapidly in the intestinal mucosa and causes transient epithelial sloughing, resulting in temporary opening of the intestinal epithelial barrier. In the present study, the rat mesenteric preparation was used to quantify the effects of the two Hbs on microvascular leakage to albumin and to investigate possible changes in the integrity of the interendothelial cell junctions and the endothelial actin cytoskeleton. In anesthetized Sprague-Dawley rats, the microvasculature of a mesenteric window was perfused with HEPES-buffered saline (HBS) containing 0.5 mg/ml BSA and 2 mg/ml alphaalpha-Hb (n = 16) or PEG-Hb (n = 5) for 2 or 10 min. Controls (n = 4) just received HBS-BSA. In some experiments (n = 9 for alphaalpha-Hb; n = 5 for PEG-Hb), the perfusate was then replaced by FITC-albumin in HBS-BSA for the next 3 min. The vasculature was then perfusion fixed, stained for filamentous actin and for mast cells, and viewed microscopically. In the remaining experiments, the mesenteric microvasculature was stained with silver nitrate to determine the number of endothelial junctional gaps per length of venules. Both Hbs increased the number and area of leaks per micrometer of venular length compared with control, but alphaalpha-Hb increased to a greater extent than PEG-Hb. Formation of leaks was accompanied by changes in the endothelial actin cytoskeleton and by an increased number of endothelial gaps. Mast cell degranulation was significantly greater ($P < 0.05$) in Hb-treated preparations compared with controls, but there was no direct correlation

between sites of degranulation and albumin leakage. These Hbs appear to induce venular leakage in the mesentery by mechanisms similar to those previously observed after treatment with histamine or nitric oxide synthase inhibitors.

L4 ANSWER 33 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:132589 HCAPLUS
DOCUMENT NUMBER: 131:430
TITLE: Cardiovascular and hemorheological effects of three modified human hemoglobin solutions in hemodiluted rabbits
AUTHOR(S): Caron, Alexis; Menu, Patrick; Faivre-Fiorina, Beatrice; Labrude, Pierre; Alayash, Abdu I.; Vigneron, Claude
CORPORATE SOURCE: Department of Hematology and Physiology, School of Pharmacy, University Henri Poincare-Nancy 1, Nancy, 54001, Fr.
SOURCE: Journal of Applied Physiology (1999), 86(2), 541-548
CODEN: JAPHEV; ISSN: 8750-7587
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The cardiovascular effects of human albumin (Alb) and three human Hb solns., dextran-benzene-tetracarboxylate Hb, αα-crosslinked Hb, and o-raffinose-polymerized Hb were compared in anesthetized rabbits undergoing acute isovolemic hemodilution with Hct reduction from 41.4 ± 2.7 to 28.8 ± 1.6%. The impact of the vasoconstricting properties of Hb was examined by measuring heart rate (HR), mean arterial pressure (MAP), abdominal aortic, and femoral arterial blood flow, vascular resistance (VR), and aortic distension during the first 3 h after hemodilution. The impact of the hemorheol. parameters was assessed by measurements of hemodiluted blood viscosity. In contrast to Alb, the Hb solns. elicited an immediate increase in MAP (20-38%). The effects of Alb and Hb solns. on HR, as well as on aortic and femoral arterial blood flow, were similar. VR decreased with Alb (20-28%) and increased with all three Hb solns. (30-90%), but the MAP and VR rising trends were different with each Hb solution Aortic distension decreased in Hb groups compared with the Alb group for the first 60 min. The viscosity of hemodiluted blood was similar for all groups at high shear rates but was dependent on the viscosity of the solns. at low shear rates. We conclude that the vasoconstriction elicited by the Hb solns. overrides the vasodilation associated with viscosity changes due to hemodilution and would be the major factor responsible to the cardiovascular changes.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:309010 HCAPLUS
DOCUMENT NUMBER: 131:134467
TITLE: Changes in the functional properties of bovine hemoglobin induced by covalent modification with polyethylene glycol
AUTHOR(S): Shorr, Robert G. L.; Kwong, Suzanna; Gilbert, Carl; Benesch, Ruth E.
CORPORATE SOURCE: Enzon, Inc., NJ, 08854-3969, USA
SOURCE: Artificial Cells, Blood Substitutes, and Immobilization Biotechnology (1999), 27(3), 185-202
CODEN: ABSBE4; ISSN: 1073-1199
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Polyethylene glycol conjugation to proteins and peptides (PEGylation) has been shown to promote increased retention time in the circulation as well as to blunt immune or allergic reactions. PEGylated bovine Hb (PEG-Hb) is

being explored in human clin. trials as an oxygen delivering agent for the sensitization of solid tumors to radiation therapy. In this study the functional properties of PEG-Hb were compared to those of bovine Hb, the mutant human Hb Rothchild and bovine Hb crosslinked between the beta chains. The rate of heme transfer from Hb to serum albumin at pH 9.0 was greatly increased by PEGylation, suggesting destabilization of the heme-globin linkage and of the bonds between αβ dimers. Measurement of oxygen binding equilibrium showed that the oxygen affinity of Hb became unusually dependent on temperature and Hb concentration after PEGylation. Evidence is presented to suggest that PEGylation of lysine β-81 at the entrance to the central cavity of the Hb tetramer might be responsible for these observations. The alterations of the functional properties of Hb induced by PEGylation are consistent with the beneficial effects of PEG-Hb in exchange transfusion and radiation sensitization models of human conditions.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 68 EMBASE

ACCESSION NUMBER: 1999309837 EMBASE

TITLE: Modified hemoglobins produce venular interendothelial gaps and albumin leakage in the rat mesentery.

AUTHOR: Baldwin A.L.

CORPORATE SOURCE: A.L. Baldwin, Department of Physiology, College of Medicine, University of Arizona, Tucson, AZ 85724-5051, United States. abaldwin@u.arizona.edu

SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (Aug 1999) Vol. 277, No. 2 46-2, pp. H650-H659. Refs: 30
ISSN: 0363-6135 CODEN: AJPPDI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
002 Physiology
029 Clinical and Experimental Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 16 Sep 1999
Last Updated on STN: 16 Sep 1999

AB Cross-linked hemoglobin (αα-Hb) and polyethylene glycol (PEG)-conjugated Hb have both been considered as possible 'blood substitutes.' Previously, we showed that PEG-Hb extravasates rapidly in the intestinal mucosa and causes transient epithelial sloughing, resulting in temporary opening of the intestinal epithelial barrier. In the present study, the rat mesenteric preparation was used to quantify the effects of the two Hbs on microvascular leakage to albumin and to investigate possible changes in the integrity of the interendothelial cell junctions and the endothelial actin cytoskeleton. In anesthetized Sprague-Dawley rats, the microvasculature of a mesenteric window was perfused with HEPES-buffered saline (HBS) containing 0.5 mg/ml BSA and 2 mg/ml αα-Hb (n = 16) or PEG-Hb (n = 5) for 2 or 10 min. Controls (n = 4) just received HBS-BSA. In some experiments (n = 9 for αα- Hb; n = 5 for PEG-Hb), the perfusate was then replaced by FITC-albumin in HBS-BSA for the next 3 min. The vasculature was then perfusion fixed, stained for filamentous actin and for mast cells, and viewed microscopically. In the remaining experiments, the mesenteric microvasculature was stained with silver nitrate to determine the number of endothelial junctional gaps per length of venules. Both Hbs increased the number and area of leaks per micrometer of venular length compared with control, but αα-Hb increased to a greater extent than PEG-Hb. Formation of leaks was accompanied by changes in the endothelial

actin cytoskeleton and by an increased number of endothelial gaps. Mast cell degranulation was significantly greater ($P < 0.05$) in Hb-treated preparations compared with controls, but there was no direct correlation between sites of degranulation and albumin leakage. These Hbs appear to induce venular leakage in the mesentery by mechanisms similar to those previously observed after treatment with histamine or nitric oxide synthase inhibitors.

L4 ANSWER 36 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:774219 HCAPLUS
DOCUMENT NUMBER: 130:29200
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules
INVENTOR(S): Hsia, Jen-chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 81 pp., Cont.-in-part of U.S. Ser. No. 482,952.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840701	A	19981124	US 1996-605531	19960222
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331
CA 2216651	A1	19961003	CA 1996-2216651	19960329
WO 9629974	A2	19961003	WO 1996-US3644	19960329
WO 9629974	A3	19970327		
W: AU, CA, CN, JP, KP, KR, MX, NZ, RU, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9666351	A	19961016	AU 1996-66351	19960329
AU 714661	B2	20000106		
EP 817628	A2	19980114	EP 1996-926048	19960329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1186431	A	19980701	CN 1996-194321	19960329
JP 11502846	T	19990309	JP 1996-529473	19960329
NZ 313806	A	20010629	NZ 1996-313806	19960329
US 6458758	B1	20021001	US 1997-824739	19970326
US 2002013263	A1	20020131	US 2001-894237	20010627

PRIORITY APPLN. INFO.:

US 1993-107543	B2	19930816
US 1994-291590	A2	19940815
US 1995-417132	A2	19950331
US 1995-482952	A2	19950607
US 1996-553196P	P	19960222
US 1996-605531	A	19960222
WO 1996-US3644	W	19960329
US 1997-824739	A1	19970326

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, particularly in cerebral ischemia in stroke, and in vivo enzyme mimics among others.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 37 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:684449 HCAPLUS
DOCUMENT NUMBER: 129:321258
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules
INVENTOR(S): Hsia, Jen-Chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5824781	A	19981020	US 1995-483283	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331
PRIORITY APPLN. INFO.:			US 1993-107543 B2	19930816
			US 1994-291590 B2	19940815
			US 1995-417132 A2	19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics among others. Examples nitroxides are TEMPOL, PROXYL, and DOXYL.
REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:650034 HCAPLUS
DOCUMENT NUMBER: 129:286015
TITLE: Compositions and methods using nitroxides in combination with biocompatible macromolecules, and use for blood substitutes, radioprotective agents, imaging agents, protectants against ischemia, and other applications
INVENTOR(S): Hsia, Jen-chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817632	A	19981006	US 1995-482437	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331

PRIORITY APPLN. INFO.: US 1993-107543 B2 19930816
US 1994-291590 A2 19940815
US 1995-417132 A2 19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics among others.

REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:604651 HCAPLUS
DOCUMENT NUMBER: 129:239892
TITLE: Compositions and methods using nitroxides in combination with biocompatible macromolecules for alleviation of radical toxicity
INVENTOR(S): Hsia, Jen-Chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5807831	A	19980915	US 1995-482951	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331

PRIORITY APPLN. INFO.: US 1993-107543 B2 19930816
US 1994-291590 A2 19940815
US 1995-417132 A2 19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics among others.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:590731 HCAPLUS
DOCUMENT NUMBER: 129:221186
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules
INVENTOR(S): Hsia, Jen-chang

PATENT ASSIGNEE(S): USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5804561	A	19980908	US 1995-480690	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331

PRIORITY APPLN. INFO.: US 1993-107543 B2 19930816
US 1994-291590 A2 19940815
US 1995-417132 A2 19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics among others.

REFERENCE COUNT: 130 THERE ARE 130 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:250729 HCAPLUS
DOCUMENT NUMBER: 128:299564
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules
INVENTOR(S): Hsia, Jen-chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5741893	A	19980421	US 1995-487496	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331

PRIORITY APPLN. INFO.: US 1993-107543 B2 19930816
US 1994-291590 B2 19940815
US 1995-417132 A2 19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents,

imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics among others. Examples are described for preparation of, e.g., nitroxide (TEMPO or PROXYL) treatment of bis(3,5-dibromosalicylyl) fumarate-crosslinked Hb.

REFERENCE COUNT: 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:175371 HCAPLUS
DOCUMENT NUMBER: 128:228010
TITLE: Methods and compositions using nitroxides combined with biocompatible macromolecules for ERI, MRI, and other applications
INVENTOR(S): Hsia, Jen-Chang
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 57 pp., Cont.-in-part of U.S. Ser. No. 417,132.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5725839	A	19980310	US 1995-482202	19950607
US 5591710	A	19970107	US 1994-291590	19940815
TW 492866	B	20020701	TW 1995-84103130	19950331
PRIORITY APPLN. INFO.:			US 1993-107543 B2	19930816
			US 1994-291590 B2	19940815
			US 1995-417132 A2	19950331

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, and in vivo enzyme mimics, among others.

REFERENCE COUNT: 146 THERE ARE 146 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 43 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:219205 HCAPLUS
DOCUMENT NUMBER: 131:13682
TITLE: Comparative assessment of 200/0.5 HAES 6% and Gelafundin in the treatment of hypovolemic in post-coronary bypass patients
AUTHOR(S): Dytkowska, Beata; Karwacki, Zbigniew; Suchorzewska, Janina; Wujtewicz, Maria
CORPORATE SOURCE: Department of Anaesthesiology and Intensive Therapy, Medical University, Gdansk, 80-211, Pol.
SOURCE: Medical Science Monitor (1998), 4(6), 1000-1003
CODEN: MSMOFR; ISSN: 1234-1010
PUBLISHER: Medical Science International Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 40 Patients after operations of coronary bypass in extracorporeal circulation were examined in order to evaluate usefulness of 200/0.5 HAES 6%

and Gelafundin. The patients were divided into 2 groups, depending on received drug (group I - HAES, group 2 - Gelafundin). A single dose of up to 15 mL/kg b. m. of colloids was given to patients with diagnosed symptoms of hypovolemic, hematocrit values over 30%. The following parameters were investigated: systolic, diastolic, mean arterial blood pressure, measured directly, as well as central venous pressure (CVP). The measurements were taken before the onset of infusion, as well as in 15, 30, 45, 60 min of infusion and 15, 30 min after its completion. Biochem. parameters such as Hb, hematocrit, number of platelets, albumin concentration, osmolality and selected blood clotting parameters were investigated before as well as 30 min after administration of the drugs. At the end of drug infusion, both groups demonstrated statistically significant increase of systolic and mean arterial blood pressure as well as central venous pressure. No significant effect of administered colloids upon biochem. parameters was observed Both HAES and Gelafundin were well tolerated by the patients. No allergic reactions were observed either during infusion or after its completion.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 68 MEDLINE on STN DUPLICATE 12

ACCESSION NUMBER: 1998225625 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9564438
TITLE: Evaluation of the oxygen delivery ability of PEG-hemoglobin in Sprague-Dawley rats during hemodilution.
AUTHOR: Conover C; Linberg R; Lejeune L; Gilbert C; Shum K; Shorr R G
CORPORATE SOURCE: Formulations-Toxicology Department, Enzon Inc., Piscataway, NJ 08854, USA.
SOURCE: Artificial cells, blood substitutes, and immobilization biotechnology, (1998 Mar) Vol. 26, No. 2, pp. 199-212. Journal code: 9431307. ISSN: 1073-1199.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 18 Jun 1998
Last Updated on STN: 18 Jun 1998
Entered Medline: 9 Jun 1998

AB Polyethylene glycol (PEG) conjugation allows bovine hemoglobin (Hb) to retain its oxygen delivery capability while increasing its plasma expansion capacity. To determine whether PEG-Hb's ability to sustain life is due to its oxygen delivery capability rather than its plasma expansion capacity, Sprague-Dawley rats were exchange-transfused up to an 85% hematocrit reduction with either PEG-Hb, PEG-50%-methemoglobin (PEG-mHb), PEG-carbon monoxide hemoglobin (PEG-COHb) or PEG-human serum albumin (PEG-HSA). Survival and respiratory rates were monitored during the exchange transfusion, at five minutes, 24 hours and 48 hours post operative. Rats surviving 14 days were evaluated for hematology, blood chemistry and histopathology. Rats infused with PEG-Hb had a survival rate of 100% during the transfusion and 79% at 24 hours, as compared to 24 hour survival rates of 30% for PEG-mHb, and 0% for both PEG-COHb and PEG-HSA. PEG-Hb treated rats that survived the 2 week observation period had normal hematological and blood chemistry levels and no significant morphological effects. Therefore, this study demonstrates that PEG-Hb can sustain life while similar plasma expansion agents with less oxygen delivery capability are not as effective.

L4 ANSWER 45 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:49265 HCAPLUS
DOCUMENT NUMBER: 126:162258
TITLE: Compositions and methods utilizing nitroxides to avoid oxygen toxicity, particularly in stabilized,

polymerized, conjugated, or encapsulated hemoglobin used as a red cell substitute

INVENTOR(S): Hsia, Jen-chang

PATENT ASSIGNEE(S): Hsia, Jen-Chang, USA

SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 107,543, abandoned.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5591710	A	19970107	US 1994-291590	19940815
TW 381022	B	20000201	TW 1993-82107408	19930909
CA 2169178	A1	19950223	CA 1994-2169178	19940816
WO 9505397	A1	19950223	WO 1994-US9246	19940816
W: CA, CN, DE, GB, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 714407	A1	19960605	EP 1994-927922	19940816
EP 714407	B1	19980211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1133050	A	19961009	CN 1994-193809	19940816
CN 1046635	B	19991124		
JP 09501681	T	19970218	JP 1995-507148	19940816
JP 3628019	B2	20050309		
EP 770627	A1	19970502	EP 1996-116519	19940816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 163186	T	19980215	AT 1994-927922	19940816
ES 2114227	T3	19980516	ES 1994-927922	19940816
US 5725839	A	19980310	US 1995-482202	19950607
US 5741893	A	19980421	US 1995-487496	19950607
US 5804561	A	19980908	US 1995-480690	19950607
US 5807831	A	19980915	US 1995-482951	19950607
US 5817632	A	19981006	US 1995-482437	19950607
US 5824781	A	19981020	US 1995-483283	19950607
US 5811005	A	19980922	US 1995-541228	19951012
US 5840701	A	19981124	US 1996-605531	19960222
US 5789376	A	19980804	US 1997-777274	19970106
US 6458758	B1	20021001	US 1997-824739	19970326
TW 529949	B	20030501	TW 1998-87112426	19980730
US 6048967	A	20000411	US 1998-128375	19980803
CN 1228962	A	19990922	CN 1999-102347	19990215
CN 1229677	A	19990929	CN 1999-102348	19990215
US 6323175	B1	20011127	US 2000-545661	20000410
US 2002013263	A1	20020131	US 2001-894237	20010627

PRIORITY APPLN. INFO.:

US 1993-107543	B2	19930816
US 1994-291590	A	19940815
EP 1994-927922	A3	19940816
WO 1994-US9246	W	19940816
US 1995-417132	A2	19950331
US 1995-482952	A2	19950607
US 1996-605531	A2	19960222
WO 1996-US3644	W	19960329
US 1997-777274	A1	19970106
US 1997-824739	A1	19970326
US 1998-128375	A3	19980803

OTHER SOURCE(S): MARPAT 126:162258

AB Compns. and processes to alleviate oxygen toxicity are disclosed based on the addition of nitroxides to physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb

solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. The formulations described herein interact with free radicals, act as antioxidant enzyme-mimics, and alleviate oxidative stress and oxygen-related toxicity. Multilamellar liposome-encapsulated Hb was prepared comprising dipalmitoyl phosphatidylcholine:cholesterol:dipalmitidyl phosphatidic acid:cholestan in a ratio of 0.5:0.4:0.2:0.07, where the cholestan was labeled with 4,4-dimethyl-3-oxazolinyloxy (I). The resonance spectrum of resulting I-cholestane labeled liposomes was shown, where nitroxide was intercalated into the liposome membrane and could be found at both the inner and outer surface of lipid bilayer water interface.

L4 ANSWER 46 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:433654 HCAPLUS
DOCUMENT NUMBER: 127:132365
TITLE: Properties of and Oxygen Binding by Albumin-Tetraphenylporphyrinatoiron(II) Derivative Complexes
AUTHOR(S): Tsuchida, Eishun; Ando, Katsutoshi; Maejima, Hiromitsu; Kawai, Noriyuki; Komatsu, Teruyuki; Takeoka, Shinji; Nishide, Hiroyuki
CORPORATE SOURCE: Department of Polymer Chemistry Advanced Research Institute for Science and Engineering, Waseda University, Tokyo, 169, Japan
SOURCE: Bioconjugate Chemistry (1997), 8(4), 534-538
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A hydrophobic tetraphenylporphyrinatoiron(II) derivative bearing a covalently bound axial imidazole [Fe(II)P] was efficiently and noncovalently bound into human serum albumin (HSA) up to an average of eight Fe(II)P mols. per HSA mol. The aqueous solns. of the HSA-Fe(II)P complex provided a reversible and relatively stable oxygen adduct under physiol. conditions (pH 7.4, and 37°). The half-life of the oxygen adduct (τ1/2) was 1 h at 37° in an air atmospheric With Fe(II)TpivPP (the so-called "picket-fence heme") having no axial base, an oxygenated HSA-Fe(II)TpivPP complex was obtained using a 20-fold molar excess of 1,2-dimethylimidazole, but the τ1/2 was very short (.apprx.10 min at 37°). The oxygen affinity [P1/2(O2)] and oxygen transporting efficiency (OTE) of HSA-Fe(II)P at 37° were 30 Torr and 22%, resp. Furthermore, the oxygen-binding and dissociation rate consts. (kon, and koff) are extremely high in comparison with those of Hb. The HSA mol. binding eight Fe(II)P mols. can transport about 3.4 mL/(dL of oxygen) under physiol. conditions,, corresponding to about 60 % of the oxygen transporting amount of human blood.

L4 ANSWER 47 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1997:560998 HCAPLUS
DOCUMENT NUMBER: 127:218342
TITLE: The effects of cross-linked hemoglobin on regional vascular conductance in dogs
AUTHOR(S): Dietz, Niki M.; Martin, Crestin M.; Beltran-Del-Rio, A. G.; Joyner, Michael J.
CORPORATE SOURCE: Department of Anesthesiology, Mayo Clinic, Rochester, MN, 55905, USA
SOURCE: Anesthesia & Analgesia (Baltimore) (1997), 85(2), 265-273
CODEN: AACRAT; ISSN: 0003-2999
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hb solns. cause systemic vasoconstriction, which might limit their use as intraoperative blood substitutes. This constriction

is thought to be caused by interaction between Hb and nitric oxide (NO). To determine whether α-α cross-linked Hb (XL-Hb) interferes with NO-mediated vasodilation caused by acetylcholine (ACh) and sodium nitroprusside (NTP), we infused these compds. into the femoral, superior mesenteric, and circumflex coronary arteries of anesthetized dogs before and after partial exchange transfusion with XL-Hb. Addnl. animals were studied after treatment with 5% albumin. XL-Hb administration increased mean arterial pressure (MAP) from 81 to 112 mmHg. Albumin reduced MAP from 84 mmHg to 76 mmHg. Vascular conductance after XL-Hb decreased in the femoral artery, was not changed in the mesenteric bed, and increased modestly in the coronary artery (from 0.19 to 0.26 mL/mmHg/min). After albumin, conductance was unchanged in the femoral artery and increased in the mesenteric artery. Conductance also increased in the coronary bed (from 0.25 to 0.49 mL/mmHg/min). The vasodilator response to ACh in the femoral or mesenteric beds was either unaffected or augmented by either XL-Hb or albumin. In the coronary bed, XL-Hb blunted the dilator responses to ACh and NTP, while albumin augmented the coronary dilator responses to ACh. In five addnl. dogs, the NO synthase inhibitor NG-monomethyl L-arginine caused MAP to increase from 85 to 90 mmHg and blunted the coronary dilator responses to ACh by approx. 25%. Subsequent XL-Hb administration caused a further increase in MAP to 112 mmHg and also further blunted ACh-mediated vasodilator responses in the coronary circulation. XL-Hb has complex effects on the circulatory system, including a reduction in the vasodilator responses to a ACh and NTP in canine coronary arteries in vivo. The potential impact of these events on patients with significant coexisting disease is unclear.

L4 ANSWER 48 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:687450 HCAPLUS
DOCUMENT NUMBER: 125:309097
TITLE: Compositions and methods utilizing nitroxides in combination with biocompatible macromolecules
INVENTOR(S): Hsia, Jen-Chang
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9629974	A2	19961003	WO 1996-US3644		19960329
WO 9629974	A3	19970327			
W: AU, CA, CN, JP, KP, KR, MX, NZ, RU, SG, US, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
TW 492866	B	20020701	TW 1995-84103130		19950331
US 5840701	A	19981124	US 1996-605531		19960222
AU 9666351	A	19961016	AU 1996-66351		19960329
AU 714661	B2	20000106			
EP 817628	A2	19980114	EP 1996-926048		19960329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 11502846	T	19990309	JP 1996-529473		19960329
NZ 313806	A	20010629	NZ 1996-313806		19960329
SG 95590	A1	20030423	SG 1998-4356		19960329
US 6458758	B1	20021001	US 1997-824739		19970326
US 2002013263	A1	20020131	US 2001-894237		20010627
PRIORITY APPLN. INFO.:			US 1995-417132	A	19950331
			US 1995-482952	A	19950607
			US 1996-553196P	P	19960222
			US 1996-605531	A	19960222

US 1993-107543	B2	19930816
US 1994-291590	A2	19940815
WO 1996-US3644	W	19960329
US 1997-824739	A1	19970326

AB Compns. and processes to alleviate free radical toxicity are disclosed based on the use of nitroxides in association with physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. Formulations are described herein that interact with free radicals, acting as antioxidant enzyme-mimics, which preserve nitroxides in their active form in vivo. Applications are described including blood substitutes, radioprotective agents, imaging agents, agents to protect against ischemia and reperfusion injury, particularly in cerebral ischemia in stroke, and in vivo enzyme mimics among others.

L4 ANSWER 49 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:294102 HCAPLUS
DOCUMENT NUMBER: 130:292429
TITLE: Process for producing human blood proteins with transgenic mammals
INVENTOR(S): Tang, Yongwei
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1114196	A	19960103	CN 1994-107317	19940701
PRIORITY APPLN. INFO.:			CN 1994-107317	19940701

AB The process comprises preparation of transgenic mammals that express the genes encoding human blood proteins and preparation of human blood proteins from the blood of the transgenic mammals. The human blood proteins consist of Hbs, albumins, C-protein, transferrin, fibrin, opsonin, prothrombin, coagulation factors, and Ig. The blood proteins are used to prepare the substitute of human blood.

L4 ANSWER 50 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:520215 HCAPLUS
DOCUMENT NUMBER: 125:212206
TITLE: Effect of oncotic pressure of diaspirin cross-linked hemoglobin (DCLHb) on brain injury after temporary focal cerebral ischemia in rats
AUTHOR(S): Cole, Daniel J.; Drummond, John C.; Patel, Piyush M.; Nary, Jeffrey C.; Applegate, Richard L. II
CORPORATE SOURCE: Departments Anesthesiology, Loma Linda University, Loma Linda, CA, 92354, USA
SOURCE: Anesthesia & Analgesia (Baltimore) (1996), 83(2), 342-347
CODEN: AACRAT; ISSN: 0003-2999
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have shown that diaspirin cross-linked Hb (DCLHb, 10 g/dL) decreases cerebral ischemia and the resultant injury in a dose-dependent manner, requiring large vols. of DCLHb for maximum efficacy. We assessed the effect of a more concentrated (20 g/dL) and more hyperoncotic preparation of DCLHb on cerebral infarction volume Immediately after middle

cerebral artery occlusion, rats were randomized to one of the following groups: Control, hematocrit not manipulated; 10/Hb, hematocrit decreased to 30% with 10% DCLHb (oncotic pressure 43 mm Hg); 7.5/Alb, hematocrit decreased to 30% with 7.5% albumin (oncotic pressure 43 mm Hg); 20/Hb, the same dose of DCLHb (20%, oncotic pressure 129 mm Hg) as the 10/Hb group (half the volume); or 15/Alb, the same dose of albumin (15%, oncotic pressure 130 mm Hg) as the 7.5/Alb group (half the volume). After 90 min of ischemia, 72 h of reperfusion was allowed. Infarction volume (mm3, mean ± SD) was less in the DCLHb groups (10/Hb = 79±17; 20/Hb = 51±14) than the oncotically matched albumin groups (7.5/Alb = 124±21; 15/Alb = 85±18) and the Control group (135±17) ($P < 0.05$). These data indicate that in this model of cerebral ischemia, DCLHb decreases ischemic brain injury more effectively than albumin, and that a hyperoncotic preparation of DCLHb is preferable.

L4 ANSWER 51 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:478442 HCAPLUS
DOCUMENT NUMBER: 122:222818
TITLE: Composition and methods using nitroxides to avoid oxygen toxicity
INVENTOR(S): Hsia, Jen-Chang
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 11
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9505397	A1	19950223	WO 1994-US9246		19940816
W: CA, CN, DE, GB, JP					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
US 5591710	A	19970107	US 1994-291590		19940815
EP 714407	A1	19960605	EP 1994-927922		19940816
EP 714407	B1	19980211			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
JP 09501681	T	19970218	JP 1995-507148		19940816
JP 3628019	B2	20050309			
ES 2114227	T3	19980516	ES 1994-927922		19940816
PRIORITY APPLN. INFO.:			US 1993-107543	A	19930816
			US 1994-291590	A	19940815
			WO 1994-US9246	W	19940816

AB This invention relates to alleviation of oxygen toxicity based on the addition of nitroxides to physiol. compatible macromols. In particular, Hb-based red cell substitutes are described featuring stable nitroxide free radicals for use in cell-free Hb solns., encapsulated Hb solns., stabilized Hb solns., polymerized Hb solns., conjugated Hb solns., nitroxide-labeled albumin, and nitroxide-labeled Ig. The formulations described herein interact with free radicals, act as antioxidant enzyme-mimics, and alleviate oxidative stress and oxygen-related toxicity.

L4 ANSWER 52 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:864541 HCAPLUS
DOCUMENT NUMBER: 123:275478
TITLE: Renal and systemic-hemodynamic response to isovolemic exchange transfusion with hemoglobin cross-linked with bis(3,5-dibromosalicyl) fumarate or albumin
AUTHOR(S): Matheson-Urbaitis, Barbara; Lu, Yuan San; Fronticelli, Clara; Bucci, Enrico
CORPORATE SOURCE: Baltimore, MD, USA
SOURCE: Journal of Laboratory and Clinical Medicine (1995),

126(3), 250-60
CODEN: JLCMAK; ISSN: 0022-2143
PUBLISHER: Mosby-Year Book
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Expts. were done in anesthetized rats to determine systemic hemodynamic and renal functional effects of isovolemic exchange transfusion with either 5% albumin or Hb cross-linked with bis (3,5-dibromosalicyl) fumarate (XLHb) in vols. ranging from 1 to 6.3 mL/100 g. Hematocrit decreased in proportion to increasing exchange vols. with either fluid. Exchange with increasing vols. of albumin led to progressive decreases in blood pressure. Exchange of 1 mL/100 g of XLHb was associated with an increase in blood pressure, whereas with larger exchanges, blood pressure returned to and was maintained at control values even for exchanges as large as 6.3 mL/100 g. An increase of similar magnitude in glomerular filtration rate occurred with both fluids. Net and fractional sodium excretion (FENa) increased significantly with both transfusion fluids; the increase was significantly larger for XLHb than for albumin. Maximal FENa excretion with albumin was about 3% but exceeded 6% with XLHb. Pretreatment with indomethacin (5 mg/kg/day for 3 days) did not blunt the diuresis that occurred with an exchange of 2 mL/100 gm XLHb. It is concluded that 5% XLHb, as compared with 5% albumin, better supports systemic blood pressure, especially as exchange volume increases, possibly as a result of Hb-induced increased vascular tone. Although a decrease in hematocrit may play a role in the diuresis observed with either fluid, the greater diuresis with XLHb must be due to some addnl. factor; the mechanism does not appear to involve prostaglandins.

L4 ANSWER 53 OF 68 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 95086633 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7994381
TITLE: Coagulation responses of human plasma after hemodilution with hemoglobin solution in-vitro.
AUTHOR: Kim H W; Awad M; Greenburg A G
CORPORATE SOURCE: Brown University, Providence, Rhode Island.
SOURCE: Artificial cells, blood substitutes, and immobilization biotechnology, (1994) Vol. 22, No. 3, pp. 613-8.
Journal code: 9431307. ISSN: 1073-1199.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199501
ENTRY DATE: Entered STN: 26 Jan 1995
Last Updated on STN: 26 Jan 1995
Entered Medline: 17 Jan 1995

AB To assess the potential for interference of Hb with the normal coagulation mechanism, we performed in-vitro hemodilution tests. Platelet rich plasma (PRP) was prepared from citrated blood samples of 5 normal volunteers diluted 3:1, 1:1, and 1:3 volume ratio with human stroma-free hemoglobin solution (SFH) or human albumin (HSA). Coagulation kinetics and clot strength were assessed with a thrombelastograph (TEG). Extrinsic and intrinsic coagulation factors were assessed measuring prothrombin time (PT) and activated partial thromboplastin time (aPTT) with an optical coagulation timer. Statistical significance was assessed using ANOVA and Neuman-Keuls tests at $p < 0.05$. At all dilutions, SFH diluted plasma showed significantly prolonged initial rate of clot formation compared to undiluted control or HSA ($p < 0.05$). However, there was no difference in formed clot strength between SFH and HSA. At high Hb concentrations Hb seems to interfere with the optical measurements of coagulation times (particularly aPTT). SFH appears to interfere with the initial phase coagulation mechanism in human plasma in-vitro; further study is needed to clarify the cause. In

measuring coagulation times of plasma containing Hb a non-optical instrument should be considered.

L4 ANSWER 54 OF 68 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 92239831 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1810487
TITLE: [The transhemenation process of bovine and human hemoglobin polymers under conditions simulating the situation in the circulatory bed].
Protsess transgemirovaniia polimerov gemoglobinov byka i cheloveka v usloviiakh, modeliruiushchikh situatsiiu v krovenosnom rusle.
AUTHOR: Smirnov I V; Khachatur'ian A A
SOURCE: Biulleten' eksperimental'noi biologii i meditsiny, (1991 Nov) Vol. 112, No. 11, pp. 500-1.
Journal code: 0370627. ISSN: 0365-9615.
PUB. COUNTRY: USSR
DOCUMENT TYPE: (COMPARATIVE STUDY)
(ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19 Jun 1992
Last Updated on STN: 19 Jun 1992
Entered Medline: 29 May 1992

AB It was shown that transhemenation, i.e. the transfer of heme from hemoglobin to human serum albumin may have the great importance in metabolism of hemoglobin. It was noted that precipitation in the case of human pyridoxal-5'-phosphate modified polyhemoglobin met-derived incubation.

L4 ANSWER 55 OF 68 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 92052646 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1946718
TITLE: The effects of alpha-alpha cross-linked hemoglobin on the feeding and locomotor activity of rats.
AUTHOR: Bauman R A; Przybelski R J; Bounds M J
CORPORATE SOURCE: Department of Medical Neurosciences Walter Reed Army Institute of Research, WRAMC, Washington, DC 20307-5100.
SOURCE: Physiology & behavior, (1991 Jul) Vol. 50, No. 1, pp. 205-11.
Journal code: 0151504. ISSN: 0031-9384.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 24 Jan 1992
Entered Medline: 17 Dec 1991

AB The feeding and locomotor activities of rats were used as an assay for the potentially toxic effects of an oxygen-carrying blood substitute. Rats lived in individual cages where they could feed ad lib by pressing a lever once for each small food pellet, drink water, or run in a wheel; a 12-h light/dark cycle was continuously in effect. After being anesthetized and hemorrhaged one-third of their total blood volume, individual rats were resuscitated with one of the following fluids: their own shed blood (OB), bis(3,5-dibromosalicylfumarate) alpha-alpha cross-linked hemoglobin (HbXL), human serum albumin (HSA), or Ringer's lactate (RL). Rats in a fifth group were not resuscitated (NR). During the dark period on the day of hemorrhage, the food intake and running activity of rats in all groups decreased. Food intake and locomotor activity of rats in the HbXL, NR and

OB groups were more suppressed than the HSA or RL groups. The food intake of rats in the HbXL and NR groups remained significantly more suppressed during the dark period of the first recovery day; running continued to be suppressed in the HbXL group on the first recovery day, but not the second recovery day. In an effort to determine the extent to which the rats in the HbXL group were impaired, an increasing number of lever presses was required for each food pellet beginning with recovery day number 3 for all treatment groups. As the ratio of presses per pellet was increased, food intake decreased and running increased for all groups; no differences between groups were significant.(ABSTRACT TRUNCATED AT 250 WORDS)

L4 ANSWER 56 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:69101 HCAPLUS
DOCUMENT NUMBER: 114:69101
TITLE: Drug delivery compositions containing coacervate systems
INVENTOR(S): Ecanow, Bernard
PATENT ASSIGNEE(S): Medaphore, Inc., USA
SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 711,066, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4963367	A	19901016	US 1987-130550	19871215
US 4738952	A	19880419	US 1985-811675	19851220
US 4849405	A	19890718	US 1986-835550	19860303
US 4914084	A	19900403	US 1987-31237	19870326
EP 274431	A2	19880713	EP 1988-300085	19880107
EP 274431	A3	19890111		
EP 274431	B1	19940504		
R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
CA 1321542	C	19930824	CA 1988-555996	19880107
AT 105183	T	19940515	AT 1988-300085	19880107
JP 63239213	A	19881005	JP 1988-2387	19880108
US 4853370	A	19890801	US 1988-182099	19880415

PRIORITY APPLN. INFO.:

US 1984-604476	B2	19840427
US 1984-604483	B2	19840509
US 1985-710048	B2	19850311
US 1985-711066	B2	19850312
US 1985-811675	A2	19851220
US 1986-835550	A2	19860303
US 1986-896844	B2	19860814
US 1987-1314	A2	19870108
US 1987-31237	A2	19870326
US 1987-54193	B2	19870526
US 1987-54194	B2	19870526
US 1984-608483	A2	19840509
US 1986-710048	B2	19860311
US 1986-711066	B2	19860312
US 1987-1814	A2	19870108
US 1987-130550	A	19871215
EP 1988-300085	A	19880107

AB A stable composition comprises particles of a coacervate-based matrix having ≥1 physiol. active compound incorporated therein and a coacervate-based encapsulating film surrounding each particles for delivery via oral, parenteral, transdermal, and transmucosal routes. The coacervate-based matrix is prepared by mixing and emulsifying a composition containing surface-active agents, water, and the active compds. to allow rapid dissoln. and smooth liberation of the active compds. The surface active

agent is selected from a protein, polymerized protein, phospholipid, polymerized phospholipid, or mixts. thereof. To 100 mL of a 10% weight/volume polymerized albumin, stroma-free Hb 10 g, glutathione 2 mM, lecithin 8 g, and 1-ethyl-3-dimethylaminopropyl carbodiimide were added and the mixture was stored at 4° for 12 h. A pH, isotonicity, and viscosity were adjusted to match those of the whole blood and the composition was filtered for use as a red blood cell substitute.

L4 ANSWER 57 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:119243 HCAPLUS
DOCUMENT NUMBER: 114:119243
TITLE: Plasma albumin repletion after transfusion with polymerized hemoglobin
AUTHOR(S): Mullins, Richard; Wehry, Mark; Hudgins, Russel; Rink, Richard
CORPORATE SOURCE: Dep. Surg., Univ. Louisville, Louisville, KY, 40292, USA
SOURCE: Journal of Surgical Research (1990), 49(5), 441-6
CODEN: JSGRA2; ISSN: 0022-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pyridoxalated polymerized Hb (PPHG) has promise as a blood substitute for transfusing patients with hemorrhage. Exchange transfusion with PPHG depletes plasma proteins. The purpose of this study was to determine if, during the early repletion of intravascular proteins, albumin was transported from the interstitium of skin or skeletal muscle into the vascular compartment. PPHG was prepared from stroma-free human Hb (100-120 mg/mL). The hematocrit of anesthetized rats dropped from 42% to 10% after exchange transfusion. Immediately postexchange, plasma albumin declined from 24 to 6 mg/mL. Five h postexchange, transfusion plasma albumin had doubled, and the skin and skeletal muscle albumin content was 80% of control. Thus, a shift of interstitial albumin from skin and skeletal muscle can rapidly replace plasma protein deficits after massive transfusion with PPHG.

L4 ANSWER 58 OF 68 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 90315456 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2369652
TITLE: Morphologic alterations in rat retina after hypervolemic infusion of cross-linked hemoglobin.
AUTHOR: Schuschereba S T; Clifford C B; Vargas J A; Bunch D; Bowman P D
CORPORATE SOURCE: Letterman Army Institute of Research, Presidio of San Francisco, CA 94129-6800.
SOURCE: Biomaterials, artificial cells, and artificial organs, (1990) Vol. 18, No. 2, pp. 299-307.
Journal code: 8802605. ISSN: 0890-5533.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 21 Sep 1990
Last Updated on STN: 21 Sep 1990
Entered Medline: 17 Aug 1990
AB Hypervolemic infusion in rats of bis (3,5-dibromosalicyl) fumarate cross-linked hemoglobin (DBBF-Hb) to 40-60% of blood volume produced histologic lesions in retina which were not observed in rats similarly infused with human serum albumin or lactated Ringer's solution. Rats treated with 40% DBBF-Hb, exhibited intermittent zones of dense retinal pigmented epithelium while 60% DBBF-Hb animals exhibited severe inner retinal edema and retinal pigmented epithelium vacuolization, large focal zones of photoreceptor outer segment disruption and in one animal,

subretinal hemorrhage. Light microscopic immunocytochemical evaluation of retinas with antibodies directed to human hemoglobin and albumin, showed the presence of both hemoglobin and albumin in this tissue. Transmission electron microscopy of the lesions demonstrated vacuolated retinal pigmented epithelial cells and large areas of focal photoreceptor outer segment disruption. We conclude that hypervolemic infusion disrupts the blood retinal barrier and that although both DBBF Hb and albumin cross, only hemoglobin produced damage in the retina.

L4 ANSWER 59 OF 68 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 90315455 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2369651
TITLE: Chronotropic effects of in vitro perfusion with albumin, stroma-free hemoglobin, and polyhemoglobin solutions.
AUTHOR: Walter S V; Chang T M
CORPORATE SOURCE: Artificial Cells and Organs Research Center, McGill University, Montreal, Quebec, Canada.
SOURCE: Biomaterials, artificial cells, and artificial organs, (1990) Vol. 18, No. 2, pp. 283-98.
Journal code: 8802605. ISSN: 0890-5533.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 21 Sep 1990
Last Updated on STN: 21 Sep 1990
Entered Medline: 17 Aug 1990

AB A negative chronotropic effect of bovine stroma-free hemoglobin was identified in spontaneously contracting myocardiocytes derived from neonatal rats. This model allowed for the evaluation of direct effects of hemoglobin solutions without the influence of hemodynamic reflexes. Significant slowing of myocardiocyte beating rates were observed from 0.8 to 11.6 g.dl-1 stroma-free hemoglobin solution. Polymerization of hemoglobin into soluble crosslinked polyhemoglobin markedly reduced its negative chronotrophic effects by more than 50% at most concentrations assayed. Chronotropic potency (% change in beating rate from baseline per g.dl-1 was significantly higher for stroma-free hemoglobin when compared to polyhemoglobin and albumin solutions. Colloid osmotic potency (% change in beating rate from baseline per mmHg) however, was similar for stroma-free hemoglobin and polyhemoglobin but significantly lower for albumin solutions. This negative chronotropic effect may in part contribute to the transient bradycardia observed following hemoglobin infusion.

L4 ANSWER 60 OF 68 EMBASE
ACCESSION NUMBER: 1990307019 EMBASE
TITLE: Major burns managed without blood or blood products.
AUTHOR: Schlagintweit S.; Snelling C.F.T.; Germann E.; Warren R.J.; Fitzpatrick D.G.; Kester D.A.; Foley B.
CORPORATE SOURCE: Department of Surgery, 910 West 10th Ave., Vancouver, B.C., V5Z 4E3, Canada
SOURCE: Journal of Burn Care and Rehabilitation, (1990) Vol. 11, No. 3, pp. 214-20.
ISSN: 0273-8481 CODEN: JBCRD2
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 024 Anesthesiology
009 Surgery
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB Four major burns (two flame, one scald, one electrical) were managed without administration of blood or plasma. Serial changes in hemoglobin, and serum albumin and total protein measurements were compared with those of controlled patients matched in age and total body surface area burned who were treated by standard methods. Hemoglobin values were lower but within one standard deviation, although serum protein and albumin measurements fell more than one standard deviation below mean values observed in control patients at comparable times after burn injury. Important treatment principles that were instrumental to recovery include a high-calorie, high-protein diet, iron supplementation, use of pediatric blood sampling techniques, and monitoring for and prophylaxis against infection while allowing eschar to separate spontaneously rather than performing early debridement. Amputation of mummified electrically burned limbs at more proximal levels, including marginally viable muscle, is recommended to minimize infection and decrease blood loss associated with customary conservative serial debridements.

L4 ANSWER 61 OF 68 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 89027172 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3179475
TITLE: Coronary flow dynamics in swine following partial exchange transfusions with hemoglobin and albumin solutions.
AUTHOR: Moores W Y; Mack R E; White F C; Bloor C M
SOURCE: Biomaterials, artificial cells, and artificial organs, (1988) Vol. 16, No. 1-3, pp. 355-6.
Journal code: 8802605. ISSN: 0890-5533.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198812
ENTRY DATE: Entered STN: 8 Mar 1990
Last Updated on STN: 8 Mar 1990
Entered Medline: 8 Dec 1988

L4 ANSWER 62 OF 68 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 87324902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3631953
TITLE: Pyridoxylated polymerized hemoglobin solution processing. Interest of a membrane molecular fractionation step.
AUTHOR: Clerc Y; Dubos M; Bihoreau N; Delamourd L; Brasseur C; Gond B; Goyffon M; Saint-Blancard J
SOURCE: Applied biochemistry and biotechnology, (1987 Apr) Vol. 14, No. 3, pp. 241-51.
Journal code: 8208561. ISSN: 0273-2289.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 5 Mar 1990
Entered Medline: 6 Oct 1987

AB Glutaraldehyde hemoglobin polymerization gives too many high polymers, resulting in a too viscous solution. We describe here an alternate method leading to superior results, as compared to the classical one. This method includes a molecular fractionation step using a tangential flow ultrafiltration that secondarily lowers the unpolymerized tetramer's content of a mildly polymerized, pyridoxylated hemoglobin solution

(Pyr-Poly Hb). This leads to an adequately polymerized product with a lesser high polymer content, implying a lower viscosity. We thus obtain a pyridoxylated, polymerized molecular fractionated solution presenting suitable features as a blood substitute: A 7.5 g% hemoglobin 2 g% albumin solution had a 16% unpolymerized tetramer's ratio, a 1.8 mPas viscosity, a P50 of 2.8 kPa, a Hill coefficient of 2.1, a binding coefficient of 1.3 mL/g, a colloid osmotic pressure of 2.4 kPa, and a methemoglobin concentration of 3% Male-Sprague-Dawley rats undergoing an isovolumic blood exchange with this Pyr-Poly Hb solution, down to a 2% hematocrit, present a mean survival time of 20 h.

L4 ANSWER 63 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1986:545942 HCAPLUS
DOCUMENT NUMBER: 105:145942
TITLE: Human hemoglobin modified by pyridoxal-5-phosphate and glutaraldehyde in the presence of serum albumin. I. Preparation and chemical properties of a new variant of infusable solution
AUTHOR(S): Fricova, Vaclava; Pristoupil, Tomas Ivan; Kramlova, Marie; Paluska, Eduard
CORPORATE SOURCE: Inst. Hematol. Blood Transfus., Prague, 128 20, Czech.
SOURCE: Biologia (Bratislava, Slovakia) (1986), 41(7), 697-704
CODEN: BLOAAO; ISSN: 0006-3088
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hb from human erythrocytes was modified by reaction with glutaraldehyde and pyridoxal-5-phosphate in the presence of human serum albumins. The reaction products were a polydisperse mixture of chemical modified Hb and serum albumins. Gel chromatog. showed the main fraction to contain mols. with mol. weight 30,000-100,000. The affinity of the modified Hb for O was lower than that of native O.

L4 ANSWER 64 OF 68 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 87099425 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3800703
TITLE: Efficacy and safety of hemoglobin-polyethylene glycol conjugate (pyridoxalated polyethylene glycol hemoglobin) as an oxygen-carrying resuscitation fluid.
AUTHOR: Iwasaki K; Iwashita Y; Ikeda K; Uematsu T
SOURCE: Artificial organs, (1986 Dec) Vol. 10, No. 6, pp. 470-4.
Journal code: 7802778. ISSN: 0160-564X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198702
ENTRY DATE: Entered STN: 2 Mar 1990
Last Updated on STN: 2 Mar 1990
Entered Medline: 13 Feb 1987
AB The safety and efficacy of a conjugate of pyridoxalated hemoglobin and polyethylene glycol (pyridoxalated PEG hemoglobin) were evaluated after administration to rats. The LD50 (lethal dose for 50% survival of group) of pyridoxalated polyethylene glycol (PEG) hemoglobin was greater than 200 ml/kg. Any pro- or anticoagulation activity was not demonstrated in in vitro coagulation tests. One day after 70% exchange-transfusion with pyridoxalated PEG hemoglobin, slight elevations of the serum glutamic-oxaloacetic transaminase, serum glutamic-pyruvic transaminase, and blood urea nitrogen values, which were 101.7 +/- 22.6 IU/L, 33.3 +/- 7.2 IU/L, and 23.1 +/- 1.4 mg/dl, respectively, were observed. However, these values were in the normal range after 3 days. With greater than 90% exchange-transfusion, all rats exchange-transfused with pyridoxalated PEG hemoglobin survived for greater than 2 weeks in contrast to the death of all the rats exchange-transfused with stroma-free hemoglobin or

albumin.

L4 ANSWER 65 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:185556 HCAPLUS
DOCUMENT NUMBER: 94:185556
ORIGINAL REFERENCE NO.: 94:30223a,30226a
TITLE: Blood circulation and oxygen supply in the body during complete replacement of blood by solutions of native and chemically modified hemoglobin
AUTHOR(S): Fedorov, N. A.; Yarochkin, V. S.; Koziner, V. B.
CORPORATE SOURCE: Cent. Inst. Hematol. Blood Transfus., Moscow, USSR
SOURCE: DHHS Publ. (NIH) (U. S.) (1980), NIH-80-1958, Blood Transfus., Blood Compon., Hepatitis, 163-9
CODEN: DPNSDO
DOCUMENT TYPE: Report
LANGUAGE: English
AB Gas exchange and hemodynamic expts. were performed on cats anesthetized with nembutal with complete (hematocrit 2 %) and partial (hematocrit 12 %) replacement of blood by solns. of native and chemical modified Hb (polyHb and polyHb albumin) of various concns. The Hb solns. were able to transfer O and maintain the life of an exsanguinated animal for several hours. The Hb solution was saturated with O in the lungs, although to a somewhat lesser extent than the Hb contained in the erythrocytes and maintained basic hemodynamic values for several hours. Attempts to increase the weight of the Hb mol. by modification of it had pos. results. The Hb prepns. were oxygenated well in the lungs but released O to the tissues less well than erythrocytic Hb. This is caused by a shift of the O dissociation curve to the left which hindered O release to the tissues because of its low partial pressure.

L4 ANSWER 66 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1980:191407 HCAPLUS
DOCUMENT NUMBER: 92:191407
ORIGINAL REFERENCE NO.: 92:30901a,30904a
TITLE: Oxygen transport and cardiovascular system function after complete blood replacement by the solutions of modified hemoglobin, polyhemoglobin, and polyhemoglobinalbumin
AUTHOR(S): Yarochkin, V. S.; Koziner, V. B.; Zeinalov, A. M.; Azhigirova, M. A.; Vyazova, E. P.
CORPORATE SOURCE: Tsentr. Inst. Gematol. Pereliv. Krovi, Moscow, USSR
SOURCE: Problemy Gematologii i Perelivaniya Krovi (1980), 25(1), 29-32
CODEN: PGPKA8; ISSN: 0552-2080
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB PolyHb and polyhemoglobinalbumin, used for complete blood replacement in cats, were better oxygenated in lungs than native Hb, but showed weaker release of O in tissues than erythrocyte Hb. Persistence in circulation of the polyHb and albumin-modified polyHb was 5- and 7-fold longer than that of native Hb. Neither blood substitute altered arterial pressure and both hemodynamic parameters for a longer time than native Hb.

L4 ANSWER 67 OF 68 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1978:500057 HCAPLUS
DOCUMENT NUMBER: 89:100057
ORIGINAL REFERENCE NO.: 89:15187a,15190a
TITLE: Comparison of cardiorespiratory effects of crystalline hemoglobin, whole blood, albumin, and Ringer's lactate in the resuscitation of hemorrhagic shock in dogs
AUTHOR(S): Nees, John E.; Hauser, Carl J.; Shippy, Clay; State, David; Shoemaker, William C.

CORPORATE SOURCE: Dep. Surg., Harbor Gen. Hosp., Torrance, CA, USA
SOURCE: Surgery (St. Louis) (1978), 83(6), 639-47
CODEN: SURGAZ; ISSN: 0039-6060
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In dogs subjected to hemorrhagic shock, hemodynamics and O transport were more improved after infusion of 500 mL of crystalline Hb, whole blood, or plasma protein fraction than after 1 L of Ringer's lactate. These responses were related to concomitant improvement in blood volume and colloid somotic pressure. Hb produced the greatest improvement, especially when
it was the first agent used after hemorrhage, apparently due to increased O affinity.

L4 ANSWER 68 OF 68 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 78075650 MEDLINE
DOCUMENT NUMBER: PubMed ID: 595109
TITLE: Total and partial blood exchange in the rat with hemoglobin prepared by crystallization.
AUTHOR: De Venuto F; Moores W Y; Zegna A I; Zuck T F
SOURCE: Transfusion, (1977 Nov-Dec) Vol. 17, No. 6, pp. 555-6.
Journal code: 0417360. ISSN: 0041-1132.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197802
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 23 Feb 1978
AB Hemoglobin, prepared by crystallization, has been used as a blood substitute in total (91 to 93%) and partial (70 to 76%) blood replacement studies. Exchange transfusions have been carried out in laboratory animals to a total blood replacement of 91 to 93 per cent with hemoglobin or with albumin solutions. When albumin was used, all animals died at approximately ten minutes after transfusion was completed, whereas all animals transfused with hemoglobin survived for five hours and displayed normal activity during this time. In these studies the plasma half-disappearance time of hemoglobin was 3.5 hours and body distribution of 51Cr-labeled hemoglobin, as a percentage of initial levels, has shown six per cent in the kidney, six per cent in the liver, 10.5 per cent in the marrow and 13 to 14 per cent in the urine at three hours after transfusion. Survival was obtained with all animals transfused with hemoglobin or albumin solutions to a partial blood replacement of 70 to 76 per cent. However, the oxygen capacity of the circulating fluid in the hemoglobin transfused animals was about three times greater than that found in the corresponding albumin-transfused controls. Values of hemoglobin, hematocrit, platelets, and P50 returned to normal pretransfusion levels within five to seven days.

=> d his

(FILE 'HOME' ENTERED AT 15:47:34 ON 03 JAN 2008)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
L1 14054 S BLOOD (W)SUBSTITUT?
L2 4447 S HEMOGLOBIN (6W) ALBUMIN
L3 105 S L1 AND L2
L4 68 DUP REM L3 (37 DUPLICATES REMOVED)

=> s hb(2w)hSA

L5 43 HB(2W) HSA

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 12 DUP REM L5 (31 DUPLICATES REMOVED)

=> d 1-12 ibib ab

L6 ANSWER 1 OF 12 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 1
ACCESSION NUMBER: 2007590575 EMBASE
TITLE: Inactivation of chosen dehydrogenases by the products of water radiolysis and secondary albumin and haemoglobin radicals.
AUTHOR: Kowalczyk A.; Serafin E.; Puchala M.
CORPORATE SOURCE: Dr. A. Kowalczyk, Department of Molecular Biophysics, University of Lodz, Lodz, Poland. olakow@biol.uni.lodz.pl
SOURCE: International Journal of Radiation Biology, (2008) Vol. 84, No. 1, pp. 15-22.
Refs: 39
ISSN: 0955-3002 E-ISSN: 1362-3095 CODEN: IJRBA3
PUBLISHER IDENT.: 781870565
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 014 Radiology
029 Clinical and Experimental Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2007
Last Updated on STN: 13 Dec 2007
AB Purpose: Inactivation of glyceraldehyde-3-phosphate dehydrogenase (GAPDH), alcohol dehydrogenase (ADH) and lactate dehydrogenase (LDH) by products of water radiolysis and by secondary radicals localized on haemoglobin (Hb) and human albumin (HSA) was studied. Materials and methods: Aqueous solutions of ADH, GAPDH and LDH were irradiated under air and under nitrous oxide (N2O) in the absence and in the presence of Hb or HSA. In order to determine the effectiveness of inactivation of the enzymes by radicals localized on Hb and HSA, the inactivation efficiency determined experimentally was compared with that calculated under assumption that only hydroxyl radicals are responsible for the enzyme inactivation. Results: In the absence of other proteins, under air, GAPDH showed the highest radiation sensitivity, followed by ADH and LDH. The sequence was reverse under anaerobic atmosphere. Oxygen increased considerably the inactivation of GAPDH and ADH. Secondary albumin and haemoglobin radicals brought about considerable inactivation of GAPGH and ADH. Albumin radicals (HSA(.)) generated under N2O inactivated GAPDH and ADH more effectively than haemoglobin radicals (Hb(.)). Under air, however, inactivation of GAPDH and ADH by haemoglobin peroxyl radicals was higher than by albumin peroxyl radicals. LDH was resistant to inactivation by haemoglobin and albumin radicals, and peroxides of these proteins. Conclusions: In the light of these results and literature data, the observed differences in the effectiveness of inactivation of the dehydrogenases studied by secondary protein radicals depend on the amino acid residues present at the active site and in its close neighborhood and on the number of amino acid residues available on the protein surface. .COPYRGT. 2008 Informa UK Ltd.

L6 ANSWER 2 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2007758815 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 18097785
TITLE: Polyethylene glycol improves conjugation of bovine hemoglobin and human serum albumin in a controlled ratio.
AUTHOR: Zheng Chunyang; Bi Jingxiu; Ma Guanghui; Su Zhiguo
CORPORATE SOURCE: National Key Laboratory of Biochemical Engineering,

Institute of Process Engineering, Chinese Academy of Sciences, Beijing, People's Republic of China.
SOURCE: Artificial cells, blood substitutes, and immobilization biotechnology, (2007) Vol. 35, No. 6, pp. 568-84. Journal code: 9431307. ISSN: 1073-1199.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-DATA-REVIEW; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 22 Dec 2007
Last Updated on STN: 22 Dec 2007

AB Direct conjugation of bovine hemoglobin (Hb) and human serum albumin (HSA) with glutaraldehyde would result in a complex mixture of dimers Hb -Hb, Hb-HSA, HSA-HSA and other oligomers. To obtain a high yield of target Hb-HSA, modulation of the reaction environment was carried out. It was found that polyethylene glycol (PEG), a hydrophilic polymer, could improve the yield of Hb-HSA conjugate. The degree of improvement depended on the molecular weight and concentration of PEG. Under optimum condition of 9% (w/v) of PEG 4000, the reaction proceeded in a controlled mode with conversion yield of starting proteins to Hb -HSA increasing from 6% to 30%. The purity was about 88% of the total conjugates. Furthermore, the impurities were mainly tetrameric molecules of two Hb-HSA conjugates. The improvement could be attributed to the "micro-compartment" created by addition of polyethylene glycol, which brings HSA and Hb close together, thus increasing the chance of conjugation between the two molecules.

L6 ANSWER 3 OF 12 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 2
ACCESSION NUMBER: 2007:286919 BIOSIS
DOCUMENT NUMBER: PREV200700290156
TITLE: The role of pH and its control on effective conjugation of bovine hemoglobin and human serum albumin.
AUTHOR(S): Zheng, Chunyang; Ma, Guanghui; Su, Zhiguo [Reprint Author]
CORPORATE SOURCE: Chinese Acad Sci, Natl Key Lab Biochem Engn, Inst Proc Engn, POB 353, Beijing 100080, Peoples R China zgsu@home.ipe.ac.cn
SOURCE: Process Biochemistry, (MAR 2007) Vol. 42, No. 3, pp. 303-309. ISSN: 1359-5113.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 2007
Last Updated on STN: 2 May 2007

AB Human serum albumin (HSA) and bovine hemoglobin (Hb) conjugate is a promising candidate as a blood substitute. However, preparation of the conjugate is problematic because both proteins tend to conjugate between themselves rather than crosslink each other. In this work, a facile process for conjugation of Hb and HSA was developed through control strategy of the reaction. The reaction was carried out in a buffer containing borax-borate and mannite. The borax-borate was used for pH buffering while mannite was used as a pH switch and a reaction promoter. As a result, self-conjugation of Hb and self-conjugation of HSA were minimized. After the one-step conjugation reaction in aqueous solution, followed by the one-step purification by ion-exchange chromatography, the conjugate of HSA and Hb was obtained with the total yield about 50%. The P-50 and the Hill coefficient for the product were 16.1 mmHg and 1.82, respectively. (c) 2006 Elsevier Ltd. All rights reserved.

L6 ANSWER 4 OF 12 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2006163843 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16321544
TITLE: Spectroscopic studies of the interaction between hypocrellin B and human serum albumin.
AUTHOR: Zhao Baozhong; Song Liming; Liu Xin; Xie Jie; Zhao Jingquan
CORPORATE SOURCE: Key Laboratory of Photochemistry, Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100080, People's Republic of China.
SOURCE: Bioorganic & medicinal chemistry, (2006 Apr 1) Vol. 14, No. 7, pp. 2428-32.
Journal code: 9413298. ISSN: 0968-0896.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200606
ENTRY DATE: Entered STN: 24 Mar 2006
Last Updated on STN: 23 Jun 2006
Entered Medline: 22 Jun 2006

AB Previous work has proved that hypocrellin B (HB) binds to human serum albumin (HSA) at a specific site instead of distributed randomly on the surface of a protein. In the current work, further investigation by using bilirubin as a site I marker indicates that HB can compete for the same site with bilirubin, suggesting that the HB binding site is located at sub-domain IIA (site I) of HSA. Moreover, bound to HSA, the HB fluorescence was found to be pH sensitive in physiological range (pH 6.0-8.0). The increasing of binding constant of HB to HSA in the pH range 6-8 also indicates that the N<-->B transition modulates the microenvironment changes of the binding site and influences considerably the binding between HB and HSA. Furthermore, picosecond time-resolved fluorescence spectra of HB -HSA complex in PBS indicate an additional short-lived component compared to that for HB in benzene, which may be assigned to the process of electron transfer from Trp-214 to HB.

L6 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:334518 HCAPLUS
DOCUMENT NUMBER: 145:262838
TITLE: Acute 40 percent exchange-transfusion with hemoglobin-vesicles (HbV) suspended in recombinant human serum albumin solution: degradation of HbV and erythropoiesis in a rat spleen for 2 weeks
AUTHOR(S): Sakai, Hiromi; Horinouchi, Hirohisa; Yamamoto, Manabu; Ikeda, Eiji; Takeoka, Shinji; Takaori, Masuhiko; Tsuchida, Eishun; Kobayashi, Koichi
CORPORATE SOURCE: Advanced Research Institute for Science and Engineering, Waseda University, Tokyo, Japan
SOURCE: Transfusion (Malden, MA, United States) (2006), 46(3), 339-347
CODEN: TRANAT; ISSN: 0041-1132
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB BACKGROUND: Hb-vesicles (HbVs; diameter, 251 ± 81 nm) are artificial O2 carriers. Their efficacy for acute exchange transfusion has been characterized in animal models. However subsequent profiles of recovery involving the degradation of HbV in the reticuloendothelial system (RES) and hematopoiesis remain unknown. STUDY DESIGN AND METHODS: Isovolemic 40 percent exchange transfusion was performed in 60 male Wistar rats with HbV suspended in 5 g per dL recombinant human serum albumin (rHSA; HbV/rHSA, [Hb] = 8.6 g/dL), stored rat RBCs suspended in rHSA (sRBC/rHSA), or rHSA alone. Hematol. and plasma biochem. analyses and histopathol. examination focusing on the spleen were conducted for the subsequent 14 days. RESULTS: The reduced hematocrit (Hct) level (26%) for the HbV/rHSA and

rHSA groups returned to its original level (43%) in 7 days. Plasma erythropoietin was elevated in all groups: the rHSA group showed the highest value on Day 1 (321 ± 123 mIU/mL) relating to the anemic conditions (HbV/rHSA, 153 ± 22; sRBC/rHSA, 63 ± 7; baseline, 21 ± 3). Simultaneously, splenomegaly occurred in all the groups as HbV/rHSA > rHSA > sRBC/rHSA. Histopathol., the accumulated HbV in the spleen was undetectable by Day 14, but hemosiderin was deposited in slight quantities for both the HbV/rHSA and sRBC/rHSA groups. Considerable amts. of erythroblasts were apparent in the spleens of both the rHSA and the HbV/rHSA groups. CONCLUSION: HbVs were phagocytized and degraded in RES, a physiol. compartment for the degradation of RBCs, and the elevated erythropoietic activity resulted in the complete recovery of Hct within 7 days in the rat model.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 12 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN DUPLICATE 4

ACCESSION NUMBER: 2006009097 EMBASE
TITLE: Replacement of rat blood with conjugate of hemoglobin and human serum albumin.
AUTHOR: Lu X.-L.; Ma T.-M.; Zheng C.-Y.; Wang Y.-Q.; Shi X.-D.; Suo X.-Y.; Yu P.-Z.; Xu Y.-H.; Su Z.-G.
CORPORATE SOURCE: Z.-G. Su, National Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing 100080, China. zgsu@home.ipe.ac.cn
SOURCE: Chinese Pharmaceutical Journal, (Oct 2005) Vol. 40, No. 19, pp. 1510-1513.
Refs: 9
ISSN: 1001-2494 CODEN: ZYZAEU
COUNTRY: China
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
LANGUAGE: Chinese
SUMMARY LANGUAGE: English; Chinese
ENTRY DATE: Entered STN: 26 Jan 2006
Last Updated on STN: 26 Jan 2006

AB OBJECTIVE: To study the effect of replacement of rat blood with the conjugate of bovine hemoglobin and human serum albumin (Hb-HSA conjugate) and other resuscitation fluids on the blood pressure and survival. METHODS: 30% or 60% of whole blood was replaced with Hb-HSA conjugate, ringer-lactate, solution, stroma-free hemoglobin (SFHb), 5% HSA in Ringer-lactate respectively. Whole blood replacement was used in blank control group and no resuscitation fluid was supplied in negative control group. Mean arterial pressure (MAP) was continuously recorded throughout the experiment. All rats were monitored for 14 d. RESULTS: For both 30% and 60% blood replacement, ringer-lactate and 5% HSA in ringer-lactate increased the MAP to a level lower than the baseline. Hb-HSA conjugate, the same as whole blood, maintains the MAP. While SFHb increased the MAP from (132.2 ± 4.0)mmHg to (139.3 ± 4.1) mmHg in 30% replacement group, but only sustained the blood pressure in the first 10 min and then decreased to lower level than the initial level in 60% replacement group. The Hb-HSA conjugate showed effectiveness with 100% survival rate (followed for 14 d), as well as whole blood replacement. CONCLUSION: The pressure change in 30% bleeding rats is more sensitive to the resuscitation fluids. The Hb-HSA conjugate maintains the MAP of bleeding rats and effectively saved bleeding rats, prior to other resuscitation fluids. The results indicate that the product is able to be a candidate as blood substitute in emergency.

L6 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2005189981 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15716124
TITLE: Binding of hypocrellin B to human serum albumin and photo-induced interactions.
AUTHOR: Zhao Baozhong; Xie Jie; Zhao Jingquan
CORPORATE SOURCE: Key laboratory of photochemistry, Center for Molecular Science, Institute of Chemistry, Chinese Academy of Sciences, Beijing, 100080, People's Republic of China.
SOURCE: Biochimica et biophysica acta, (2005 Mar 11) Vol. 1722, No. 2, pp. 124-30. Electronic Publication: 2004-12-31. Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200505
ENTRY DATE: Entered STN: 13 Apr 2005
Last Updated on STN: 11 May 2005
Entered Medline: 10 May 2005

AB Molecular binding of hypocrellins to human serum albumin (HSA) needs to be further clarified considering the phototherapeutic potentials of hypocrellins to vascular diseases. In the current work, it was estimated that the binding constant of hypocrellin B (HB) to HSA was 2.28 x 10(4) M(-1). Furthermore, based on the fluorescence responses for both HB and the tryptophan of HSA, it was suggested that the binding of HB to HSA should be more specific rather than distributed randomly on the surface of HSA, which was also confirmed by photobleaching of the tryptophan via photosensitization of HB. Besides, it was found that both of the photo-bleaching of the tryptophan and the photo-oxidation of HB were principally oxygen-dependent, suggesting reactive oxygen species generated via the photosensitization of HB, instead of the free radicals of the photosensitizer (HB*-), play the most important role in photodynamic processes.

L6 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2005312309 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15960074
TITLE: Conjugate of bovine hemoglobin and human serum albumin as a candidate for blood substitute: characteristics and effects on rats.
AUTHOR: Lu Xiu-Ling; Zheng Chun-Yang; Xiao-DongShi; Wang Yong-Quan; Suo Xiao-Yan; Yu Peng-Zhan; Xu Yu-Hong; Ma Tie-Min; Su Zhi-Guo
CORPORATE SOURCE: National Key Laboratory of Biochemical Engineering, Institute of Process Engineering, Chinese Academy of Sciences, Beijing, China.
SOURCE: Artificial cells, blood substitutes, and immobilization biotechnology, (2005) Vol. 33, No. 2, pp. 83-99. Journal code: 9431307. ISSN: 1073-1199.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200510
ENTRY DATE: Entered STN: 18 Jun 2005
Last Updated on STN: 8 Oct 2005
Entered Medline: 7 Oct 2005

AB Conjugate of bovine hemoglobin (bHb) and human serum albumin (HSA) was prepared. The product was simply composed of 89.7% one-to-one Hb -HSA conjugate, 6.0% oligomer of Hb and HSA, 3.5% unconjugated HSA and 0.8% unconjugated Hb, with an average molecular weight of 157 kD. The physicochemical characteristics were determined. Effects of single replacement on blood pressure and long-term survival of

rats with 30% and 60% acute blood loss were studied, in comparison with Ringer-lactate solution, stroma-free hemoglobin (SFHb), 5% HSA in Ringer-lactate, whole blood and no resuscitation fluid. Results showed that Hb-HSA conjugate maintained the mean arterial pressure of rats to initial level with no pressor effect. Long-term effects of the replacement fluids on 30% bleeding rats showed that, for the group infused with Hb-HSA conjugate, histology of five major organs, heart, kidney, liver, spleen and lung, were essentially normal, similar to that of whole blood, while obviously renal side-effects appeared in other groups. The efficacy of the conjugate was further demonstrated by the resuscitation of lethal hemorrhagic shock rats (60% acute blood loss) with 100% survival rate (followed for 14 days), the same result as whole blood. The Hb-HSA conjugate can thus be another candidate for blood substitute in emergency.

L6 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001645009 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11697451
TITLE: Biological monitoring in workers in a nitrobenzene reduction plant: haemoglobin versus serum albumin adducts.
AUTHOR: Thier R; Lewalter J; Selinski S; Bolt H M
CORPORATE SOURCE: Department Physiology and Pharmacology, University of Queensland St. Lucia, QLD 4072, Australia.
SOURCE: International archives of occupational and environmental health, (2001 Sep) Vol. 74, No. 7, pp. 483-8. Journal code: 7512134. ISSN: 0340-0131.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 8 Nov 2001
Last Updated on STN: 28 Jan 2002
Entered Medline: 24 Jan 2002

AB The high priority of monitoring workers exposed to nitrobenzene is a consequence of clear findings of experimental carcinogenicity of nitrobenzene and the associated evaluations by the International Agency for Research on Cancer. Eighty male employees of a nitrobenzene reduction plant, with potential skin contact with nitrobenzene and aniline, participated in a current medical surveillance programme. Blood samples were routinely taken and analysed for aniline, 4-aminodiphenyl (4-ADP) and benzidine adducts of haemoglobin (Hb) and human serum albumin (HSA). Also, levels of methaemoglobin (Met-Hb) and of carbon monoxide haemoglobin (CO-Hb) were monitored. Effects of smoking were straightforward. Using the rank sum test of Wilcoxon, we found that very clear-cut and statistically significant smoking effects (about 3-fold increases) were apparent on CO-Hb ($P = 0.00085$) and on the Hb adduct of 4-ADP ($P = 0.0006$). The mean aniline-Hb adduct level in smokers was 1.5 times higher than in non-smokers; the significance ($P = 0.05375$) was close to the 5% level. The strongest correlation was evident between the Hb and HSA adducts of aniline ($r(s) = 0.846$). Less pronounced correlations (but with P values < 0.02) appeared between aniline-Hb and 4-ADP-Hb adducts ($r(s) = 0.388$), between 4-ADP and 4-ADP-HSA adducts ($r(s) = 0.373$), and between 4-ADP-Hb and aniline-HSA adducts ($r(s) = 0.275$). In view of the proposal for additional use of the aniline-HSA adduct for biological monitoring, particularly in cases of acute overexposures or poisonings, the strong correlation of the Hb and HSA conjugates is noteworthy; the ratio aniline-HSA:aniline-Hb was 1:42 for the entire cohort.

L6 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000484487 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10988313

TITLE: In vivo effects of Hb solutions on blood viscosity and rheologic behavior of RBCs: comparison with clinically used volume expanders.
AUTHOR: Menu P; Bleeker W; Longrois D; Caron A; Faivre-Fiorina B; Muller S; Labrude P; Stoltz J F
CORPORATE SOURCE: Departments of Physiology and Angiohematology-Hemorheology, Henri Poincare University, Nancy, France.. menu@pharma.u-nancy.fr
SOURCE: Transfusion, (2000 Sep) Vol. 40, No. 9, pp. 1095-103. Journal code: 0417360. ISSN: 0041-1132.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200010
ENTRY DATE: Entered STN: 19 Oct 2000 Last Updated on STN: 19 Oct 2000 Entered Medline: 10 Oct 2000

AB BACKGROUND: Hb-based oxygen carriers (HbOCs) have vasoactive effects that are still poorly understood. Factors known to have vasoactive effects, such as plasma, whole-blood viscosity, and the rheologic behavior of RBCs, are modulated by HbOCs in vitro, but few in vivo studies have been performed. STUDY DESIGN AND METHODS: Rabbits were phlebotomized (30%) and resuscitated with unmodified stroma-free Hb (SFHb), dextran-tetracarboxylate-Hb (Dex-BTC-Hb), O-raffinose-polymerized Hb (OrpHb), HSA, or hydroxyethyl starch 200 (HES). Plasma viscosity was assessed with a capillary viscometer and whole-blood viscosity with a rotational viscosimeter. RBC aggregation kinetics were determined by analysis of back-scattered light in a rotating device. RESULTS: As compared to that in the control RBC suspension, resuscitation with SFHb, OrpHb, or HSA decreased plasma and whole-blood viscosity as well as RBC aggregation; resuscitation with Dex-BTC-Hb increased whole-blood viscosity at low shear rates as well as RBC aggregation, whereas that with HES decreased whole-blood viscosity but increased RBC aggregation. CONCLUSION: HbOCs have different rheologic effects in vitro and in vivo. There are marked differences among the Hb solutions in their in vivo effects on viscosity and RBC rheologic behavior (especially at low shear rates encountered in the venous circulation and the microcirculation), which may be related to the chemical modifications applied to hemoprotein. These results could contribute to an understanding of the vasoactive effects of HbOCs.

L6 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999308931 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10381201
TITLE: Damage to hemoglobin by radiation-generated serum albumin radicals.
AUTHOR: Puchala M; Szweda-Lewandowska Z
CORPORATE SOURCE: Department of Molecular Biophysics, University of Lodz, Poland.
SOURCE: Free radical biology & medicine, (1999 May) Vol. 26, No. 9-10, pp. 1284-91. Journal code: 8709159. ISSN: 0891-5849.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO) Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 21 Sep 1999 Last Updated on STN: 21 Sep 1999 Entered Medline: 9 Sep 1999

AB We have studied the effects of the interaction of radiation generated

human serum albumin radicals (HSA*) with human hemoglobin molecules (Hb). Diluted Hb aqueous solutions were irradiated under N2O or argon without HSA and in the presence of HSA. Analysis of Hb absorbance spectra in the visible range, cross-linking of HSA* radicals with Hb molecules and functional properties of Hb were investigated. The degree of Hb destruction estimated on the basis of changes in the absorption spectra indicated that the effectiveness of HSA* radicals generated under N2O for Hb destruction was approximately equal to that of *OH radicals. In this case mainly *OH radicals formed the secondary HSA* radicals. However, during the irradiation Hb + HSA under argon the presence of equivalent amounts of oxidizing and reducing products of water radiolysis lowers the degree of Hb destruction. Some reactions of HSA* radicals with Hb molecules lead to the formation of covalent bonds between the molecules of both proteins. The following types of hybrids could be distinguished: Hb monomer-HSA, Hb dimer-HSA and higher aggregates. Structural changes of Hb by HSA* radicals were reflected by alterations in the oxygen affinity (increase) and cooperativity (decrease) of Hb. The results obtained indicate that in the experimental systems studied, the HSA* radical reactions with Hb molecules are favoured over recombination reactions of HSA* radicals. On this basis one can suggest that in the studied systems Hb plays the role of an acceptor of radical energy located on HSA.

L6 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN DUPLICATE 10

ACCESSION NUMBER: 1997:200704 BIOSIS
DOCUMENT NUMBER: PREV199799499907
TITLE: Hemoglobin-induced contraction of pig pulmonary veins.
AUTHOR(S): Muldoon, Sheila M. [Reprint author]; Ledvina, Mary Ann; Hart, Jayne L.; MacDonald, Victor W.
CORPORATE SOURCE: Dep. ANE, USUHS, 4301 Jones Bridge Rd., Bethesda, MD 20814, USA
SOURCE: Journal of Laboratory and Clinical Medicine, (1996) Vol. 128, No. 6, pp. 579-584.
CODEN: JLCMAK. ISSN: 0022-2143.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 May 1997
Last Updated on STN: 12 May 1997

AB The effects of hemoglobin A-o (HbA-o), alpha-alpha cross-linked hemoglobin (alpha-alpha-Hb), cyanomet alpha-alpha cross-linked hemoglobin (cyanomet-alpha-alpha-Hb), and human serum albumin (HSA) were compared under basal conditions and during relaxation with acetylcholine (ACh), sodium nitroprusside (SNP), and papaverine (PAP) in porcine pulmonary veins. Isometric tension changes were recorded in isolated rings (3 to 4 mm) that were suspended in Krebs solution bubbled with 95% O-2/5% CO-2. Increasing concentrations of HbA-o and alpha-alpha-Hb (10-9 - 3 times 10-6 mol/L) caused-concentration-dependent increases in tension that reached a maximum of 4.20 +- 0.3 gm and 3.78 +- 0.6 gm, respectively. Cyanomet-alpha-alpha-Hb and HSA (10-9 - 3 times 10-6 mol/L) did not cause significant increases in tension. The maximum responses to HbA-o and alpha-alpha-Hb were significantly increased during relaxation with ACh and SNP but not with PAP. In contrast, SNP (10-4 mol/L) and PAP (10-5 mol/L), but not ACh, reversed contractions induced by HbA, and alpha-alpha-Hb. These studies support the concept that hemoglobin-induced vascular contraction is primarily mediated by inactivation of the vasodilator nitric oxide in vitro. We suggest that this mechanism is common to acellular hemoglobins in which the ligand binding site is unimpaired and in which the heme iron is in the ferrous (+2) state.

=> e su z/au
E1 7 SU YVONNE C F/AU

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E2            1      SU YY/AU
E3          957 --> SU Z/AU
E4           11      SU Z A/AU
E5          280      SU Z B/AU
E6           28      SU Z C/AU
E7           89      SU Z D/AU
E8           49      SU Z F/AU
E9          199      SU Z G/AU
E10         119      SU Z H/AU
E11           1      SU Z I/AU
E12           1      SU Z I FEN/AU

=> s s e3
L7            0 S "SU Z"/AU

=> s  e3
L8          957 "SU Z"/AU

=> e xiuling l/au
E1            1      XIULING H/AU
E2            1      XIULING JIN/AU
E3            7 --> XIULING L/AU
E4            1      XIULING LI/AU
E5            1      XIULING LIN/AU
E6            1      XIULING W/AU
E7            3      XIULING WANG/AU
E8            2      XIULING X/AU
E9            2      XIULING XU/AU
E10           1      XIULING XUE/AU
E11           1      XIULING Z/AU
E12           1      XIULONG/AU

=> s e3
L9            7 "XIULING L"/AU

=> e chunyang z/au
E1            2      CHUNYANG LIU/AU
E2            1      CHUNYANG LU/AU
E3            1 --> CHUNYANG Z/AU
E4            1      CHUNYAO T/AU
E5            1      CHUNYAO WU/AU
E6            1      CHUNYAYEV OLEG NIKOLAYEVICH/AU
E7            1      CHUNYAYEVA LIDIYA OMOVNA/AU
E8            1      CHUNYEN P/AU
E9            1      CHUNYI GAO/AU
E10           1      CHUNYI MA/AU
E11           1      CHUNYI N/AU
E12           3      CHUNYI W/AU

=> s e3
L10           1 "CHUNYANG Z"/AU

=> yuhong x/au
YUHONG IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> e yuhong x/au
E1            1      YUHONG WANG/AU
E2            1      YUHONG WU/AU
E3            3 --> YUHONG X/AU
E4            1      YUHONG Y/AU
E5            1      YUHONG Z/AU
```

```
E6            2      YUHONG ZHANG/AU
E7            1      YUHONG ZHAO/AU
E8            1      YUHOS CSABA/AU
E9            1      YUHOS R/AU
E10           1      YUHOSZ M D/AU
E11           1      YUHOU CHEN/AU
E12           1      YUHOU FAN/AU

=> s e3
L11           3 "YUHONG X"/AU

=> d his

     (FILE 'HOME' ENTERED AT 15:47:34 ON 03 JAN 2008)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
L1         14054 S BLOOD (W)SUBSTITUT?
L2          4447 S HEMOGLOBIN (6W) ALBUMIN
L3           105 S L1 AND L2
L4            68 DUP REM L3 (37 DUPLICATES REMOVED)
L5            43 S HB(2W)HSA
L6            12 DUP REM L5 (31 DUPLICATES REMOVED)
                 E SU Z/AU
L7             0 S S E3
L8           957 S  E3
                 E XIULING L/AU
L9             7 S E3
                 E CHUNYANG Z/AU
L10            1 S E3
                 E YUHONG X/AU
L11            3 S E3

=> s l8 or l9 or l10 or l11
L12          968 L8 OR L9 OR L10 OR L11

=> s l4 or l6
L13           77 L4 OR L6

=> s l12 and l13
L14            0 L12 AND L13

=> d his

     (FILE 'HOME' ENTERED AT 15:47:34 ON 03 JAN 2008)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 15:48:02 ON 03 JAN 2008
L1         14054 S BLOOD (W)SUBSTITUT?
L2          4447 S HEMOGLOBIN (6W) ALBUMIN
L3           105 S L1 AND L2
L4            68 DUP REM L3 (37 DUPLICATES REMOVED)
L5            43 S HB(2W)HSA
L6            12 DUP REM L5 (31 DUPLICATES REMOVED)
                 E SU Z/AU
L7             0 S S E3
L8           957 S  E3
                 E XIULING L/AU
L9             7 S E3
                 E CHUNYANG Z/AU
L10            1 S E3
                 E YUHONG X/AU
L11            3 S E3
L12          968 S L8 OR L9 OR L10 OR L11
```

L13 77 S L4 OR L6
L14 0 S L12 AND L13

	Document ID	Kind Codes	Source	Issue Date	Pages
88	US 4061466 A		USPAT	19771206	8

	Title
88	Biologically active composition and the use thereof

	Document ID	Kind Codes	Source	Issue Date	Pages
1	US 20070065838 A1		US-PGPUB	20070322	31
2	US 20070054313 A1		US-PGPUB	20070308	31
3	US 20070031878 A1		US-PGPUB	20070208	67
4	US 20070009930 A1		US-PGPUB	20070111	66
5	US 20060247423 A1		US-PGPUB	20061102	11
6	US 20060223143 A1		US-PGPUB	20061005	66
7	US 20060166225 A1		US-PGPUB	20060727	67
8	US 20060142950 A1		US-PGPUB	20060629	67
9	US 20060084091 A1		US-PGPUB	20060420	67
10	US 20060051795 A1		US-PGPUB	20060309	31
11	US 20050191688 A1		US-PGPUB	20050901	57
12	US 20030054390 A1		US-PGPUB	20030320	31
13	US 20030027156 A1		US-PGPUB	20030206	73
14	US 20020183934 A1		US-PGPUB	20021205	53
15	US 20020051976 A1		US-PGPUB	20020502	76
16	US 7058515 B1		USPAT	20060606	65

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	2788	blood adj3 substitut$3	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:56
L2	133250	hemoglobin (3w) albumin	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:56
L3	783	l1 same l2	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:57
L4	404	l3 same (human serum adj albumin)	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:57
L5	88	l3 same (human adj serum adj albumin)	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:57
L6	128602	SU XIULING CHUNYANG	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:59
L7	27	l5 and l6	US-PGPUB; USPAT	OR	OFF	2008/01/03 15:59